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MANAGEMENT OF PATIENTS WITH CHRONIC RENAL DISEASE. By THEODORE C. JANEWAY, M.D. 157

THE RELATION OF PROGNOSTIC FACTORS TO TREATMENT IN DIABETES MELLITUS. By NELLIS B. FOSTER, M.D. 176

THE EFFECT OF EXERCISE UPON CARBOHYDRATE TOLERANCE IN DIABETES. By THEODORE B. BARRINGER, JR., M.D. 181

SOME ASPECTS OF THE CLINICAL STUDY OF THE RESPIRATION: THE SIGNIFICANCE OF ALVEOLAR AIR ANALYSES. By FRANCIS W. PEABODY, M.D. . . . 184

HISTORICAL SKETCH OF THE DEVELOPMENT OF THE DUODENAL TUBE. By MAX EINHORN, M.D. 202

TONSILLAR ENDAMEBIASIS AND THYROID DISTURBANCES. By J. S. EVANS, M.D., WM. S. MIDDLETON, M.D., and ALLEN J. SMITH, M.D. 210

PATHOGNOMONIC ALTERATIONS OF THE CEREBROSPINAL FLUID IN SYPHILIS OF THE NERVOUS SYSTEM. By JOSEPH COLLINS, M.D. 222

SPONTANEOUS PNEUMOTHORAX. By LOUIS HAMMAN, M.D. 229

THE OCCURRENCE OF ARTERITIS IN MENINGITIS. By J. W. McMEANS, M.D. . . . 249

THE ROENTGEN EXPERT WITNESS. By EDWARD HOLMAN SKINNER, M.D. . . . 257

A CLINICAL STUDY OF CHRONIC DIARRHEA. By DUDLEY ROBERTS, M.D. . . . 259

THE METABOLISM IN A CASE OF MYASTHENIA GRAVIS, WITH CONSIDERATIONS OF THE ADMINISTRATION OF CALCIUM AND OF GLANDULAR PREPARATIONS. By ARTHUR BOOKMAN, M.D., and ALBERT A. EPSTEIN, M.D. 267

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CONTENTS

ORIGINAL ARTICLES

Management of Patients with Chronic Renal Disease 157
By Theodore C. Janeway, M.D., Baltimore, Maryland.

The Relation of Prognostic Factors to Treatment in Diabetes Mellitus . 176
By Nellis B. Foster, M.D., New York.

The Effect of Exercise upon the Carbohydrate Tolerance in Diabetes . 181
By Theodore B. Barringer, Jr., M.D., New York.

Some Aspects of the Clinical Study of the Respiration: The Significance of Alveolar Air Analyses 184
By Francis W. Peabody, M.D., Boston, Massachusetts.

Historical Sketch of the Development of the Duodenal Tube 202
By Max Einhorn, M.D., Professor of Medicine at the New York Post-graduate Medical School, New York.

Tonsillar Endamebiasis and Thyroid Disturbances 210
By J. S. Evans, M.D., Wm. S. Middleton, M.D., Madison, Wisconsin, and Allen J. Smith, M.D., Philadelphia.

Pathognomonic Alterations of the Cerebrospinal Fluid in Syphilis of the Nervous System 222
By Joseph Collins, M.D., Physician to the Neurological Institute, New York.

Spontaneous Pneumothorax 229
By Louis Hamman, M.D., Baltimore, Maryland.

The Occurrence of Arteritis in Meningitis 249
By J. W. McMeans, M.D., R. B. Mellon Fellow in Pathology, University of Pittsburgh.

The Roentgen Expert Witness 257
By Edward Holman Skinner, M.D., Kansas City, Mo.

A Clinical Study of Chronic Diarrhea 259
By Dudley Roberts, M.D., Attending Physician, Brooklyn Hospital; Consulting Gastro-enterologist, King's Park State Hospital and Coney Island Hospital, Brooklyn, New York.

The Metabolism in a Case of Myasthenia Gravis, with Considerations of the Administration of Calcium and of Glandular Preparations . . 267
By Arthur Bookman, M.D., and Albert A. Epstein, M.D., New York.

REVIEWS

Principles of Human Physiology. By Ernest H. Starling, M.D. (Lond.), F.R.C.P., F.R.S., Hon. M.D. (Breslau), Hon. Sc.D. (Cambridge and Dublin) 275
Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., and Leighton F. Appleman, M.D. . . 276
Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., and Leighton F. Appleman, M.D. . . 276
Notes on Dental Metallurgy. By W. Bruce Hepburne, L.D.L. (Glasgow) 277
The House-fly, Musca Domestica Linn. Its Structure, Habits, Development, Relation to Disease and Control. By C. Gordon Hewitt. . 278
A Text-book of Medical Chemistry and Toxicology. By James W. Holland, M.D. 278
Roentgen Rays: How to Produce and Interpret Them. By Harold Mowat, M.D. (Edin.) 279
Headache. By Dr. Siegmund Auerbach 279
Human Physiology. By Luigi Luciani 280
An Essay on Hasheesh, Including Observations and Experiments. By Victor Robins 280

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

The European Bed-bug as a Carrier of Disease 281
The Relation of Bile Pigments to Hemoglobin 282
An Improvement in the Phenolphthalein Test for Occult Blood in the Feces 282
Observations on Infection and Immunity in Maternal and Fetal Lues . 283
Vaccination Against Typhoid in the United States Army 284

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

Gastrostomy for Stomach Drainage 285
A Review of the Literature of Fractures 286
Banti's Disease 286
Operative Treatment of Tumors of the Bladder 287
Errors in Diagnosis of Renal and Ureteral Calculus 287
Shock and Hemorrhage: An Experimental Study 288
A Radical Operation for Hemorrhoids by a Simple Suture 289
Eckehorn's Operation for Prolapsus Ani in Adults 289
Gastric Fistula with Suction Drainage for Atonic Conditions of the Stomach and Intestine 290

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Is There a Successful Treatment of Scarlet Fever 291
Intravenous Iodid Therapy 291
Report on the Allen Treatment of Diabetes 292
Clinical Studies in Caffein 292
Emetin Hydrochloride 294
Specific Treatment in Typhoid Fever 294
Concerning Exercise in the Treatment of Severe Diabetes 294
Poisoning by Mercuric Chlorid and its Treatment 295
Coagulen in the Treatment of Pulmonary Hemorrhage 296
A Study of Different Nitrogenous Diets in Chronic Nephritis 296

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M.D.

Treatment of Infantile Beriberi 297
Serum Treatment of Scarlet Fever 297
Influenza Meningitis 298
Prophylaxis in Pediatrics; Institutional 299

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

The Treatment of Abortion Complicated by Fever 299
Auto-infection 300

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Treatment of Uterine Perforation—Radical or Conservative 303
Treatment of Pelvic Inflammation with Ultraviolet Rays 304
Ovarian Transplantation 305

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.

Mastoiditis and Erysipelas 306
Massage of the Tympanopharyngeal Tube 307
Mastisol 307
Good Hearing after Total Destruction of the Mastoid Process by Means of a Projectile. Total Deafness, Traumatic Rupture of the Drumhead and Complete Facial Paralysis following Concussion of the Mastoid Process 308

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P., AND OSKAR KLOTZ, M.D., C.M.

The Influence of the Exposure of the Roentgen-rays upon the Formation of Antibodies 309
Further Investigations into the Etiology of the Protozoan Disease of Turkeys, known as Black Head 310
The Sterility of Bile under Normal Conditions 310
Contribution to the Study of Endemic Goitre 310
Basedow's Disease and the Thymus 311
A Bacterial Study of an Epidemic of Septic Sore Throat 311
The Relation of the Adrenals to Cholesterin Metabolism 312

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

FEBRUARY, 1916.

ORIGINAL ARTICLES

MANAGEMENT OF PATIENTS WITH CHRONIC RENAL DISEASE.[1]

By Theodore C. Janeway, M.D.,

BALTIMORE, MARYLAND.

(From the Medical Clinic of the Johns Hopkins Hospital.)

It needs only a glance at current medical periodicals to show the amount of time and energy being devoted to the study of kidney function today. In fact, some may have been inclined to believe that the 'phthalein test and the electrocardiograph are the only methods now employed in the investigation of patients in our hospitals. So much work may surely, by this time, be expected to have produced some results which the practitioner of medicine can use for the good of his patients. It has been my fortune during this period of the development of functional tests, both at the Presbyterian Hospital, New York, and during the last year at the Johns Hopkins Hospital, to have for my associates a group of men actively interested in this field. During the last year, especially, Dr. Mosenthal and Dr. Rowntree and their co-workers in our clinic have, by their laboratory studies, quite definitely modified our practice in the wards. I shall give our present views on the practical management of the different types of chronic renal disease which are commonly met in general practice. I say "practical management of the patient," because, except in the rarest instances, we have no real treatment of the disease. We

[1] Read before the Academy of Medicine, New York City, November 4, 1915.

must not let the fascination of growing insight into the complexities of function blind us to the fact that the problem of fundamental importance in any disease is the problem of its cause. It is devoutly to be hoped that our knowledge may be increased along this line. The study of the relation of focal infections to renal disease is a promising movement, but a vast material must be worked over critically before we can reach conclusions. Except for certain cases of renal involvement in secondary syphilis, possibly rare cases of nephritis due to malaria, lead poisoning, pregnancy, or some focus of streptococcus infection, we can not speak of an effective causal therapy of chronic nephritis.

For the most part, treatment has in the past been purely schematic and based on a conventional diagnosis. Since this treatment usually involved violent interference with the habits of a lifetime, even though it did not use dangerous drugs, we can not regard it as a harmless procedure. To tell every patient with albuminuria or hypertension to stop eating red meat, or still worse, as I have actually seen done, to go on a milk diet, is evidence either of colossal ignorance or of inexcusable mental laziness. Nothing is clearer to me, however, in dealing with patients who have a chronic disease than the amount of thought and tact necessary to accomplish the readjustment of their life to the necessary limitations which they must be taught to recognize. This is a field which the internist has to himself, and it should be our pride to develop it in detail as carefully as the surgeon has developed his operative technic. Here is where the functional test becomes indispensable.

The treatment of chronic disease has two aims: the prolongation of life, and the amelioration of the discomforts due to the disease. These two aims are achieved by two types of treatment: (1) safeguarding treatment, which aims to protect a weakened function from further damage by overstrain; (2) symptomatic treatment, directed toward the amelioration of the symptoms which depend upon disordered function. While a correct anatomical diagnosis is always desirable it is not of special importance in determining treatment along either of these lines. What is fundamental is the accurate estimation of the kind and degree of functional damage.

Chronic renal disease presents an endless variety of symptom combinations, but certain clinical types occur with such frequency that we are all called on to meet the problem of their management; and they present themselves, in a way, as specific practical problems. I propose to consider them as such:

1. Patients in whom albumin and casts in the urine are the only evidence of disease. This is a large group. These patients come to us, both family practitioners and consultants, from the life insurance examiners; or if we have careful patients, and are careful examiners, we discover them among our supposedly healthy clients. They are found among the children in the clinics. Their problem is the

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last problem we have to work out in a convalescent from known acute nephritis or from a pregnancy albuminuria. The last two instances give the key to the important question that must be answered for every patient in this group, namely, Are the albumin and casts in the urine the last remaining evidences of a healing renal lesion? A searching inquiry must be made into the history for evidences of a mild unrecognized scarlet fever, a tonsillitis, or other infection, recent pregnancy, syphilis, the administration of salvarsan, or some intoxication which might have led to acute renal disease without noticeable symptoms. If such possible cause can be found, or even suspected, especially in the case of young people, then a period of rest in bed and milk or bland diet should be given a thorough trial. If treatment, as of true acute nephritis, results in steady subsidence of the albuminuria, then it should be persisted in just as though the patient had a known acute nephritis. No sacrifice is too great for any patient to make which may prevent the subsequent development of chronic diffuse nephritis, leading to the secondary contracted kidney in later life. If, however, there is no suspicion of a past or existing infection, and if a week in bed on milk diet has no appreciable effect upon the albumin and casts, then bed and milk diet are an unwarrantable hardship, because they are sacrifice without result. If persisted in, the result will very likely be the sacrifice of the physician.

In children the next problem is the differentiation of postural albuminuria. This is much commoner than is usually supposed, and marked albuminuria without casts, or with rare casts, in a child should always suggest the possibility of its being this peculiar type. For an excellent discussion of this subject I can recommend the article by Langstein in *Pfaundler and Schlossman's Handbuch*,[2] for interesting special pleading on the two sides of the question, the monographs of Politzer and of Jehle.[3]

Testing the separate urines passed at different times of day, and the effect of standing fifteen to thirty minutes in marked lordotic position, will often clear up the diagnosis promptly. The large amount of protein precipitable by acetic acid in the cold has been, in my experience, an important feature of the albuminous urine in these cases. The treatment of these children should, I believe, be along the lines of general invigoration, with medical gymnastics for the improvement of posture. Their diet should be ample, not restricted. In some the suspicion of true nephritis is strong, though there is marked postural albuminuria. Such cases should be more cautiously handled.

[2] Langstein, L., Die orthotische Albuminurie, Handbuch, Pfaundler und Schlossman, 1910, iv, 30. F. C. W. Vogel, Leipzig.

[3] Ren juvenum, Beiträge zur Kenntnis der orthostatischen Albuminurie, Berlin und Wien, 1913, Urban und Schwarzenburg; Die Albuminurie, Julius Springer, Berlin, 1914.

When one has clearly recognized and separated from the patients in whom albuminuria has been accidentally discovered these two preceding types, residual albuminuria after acute nephritis and postural albuminuria, there remain the large number of patients in whom the cause of the albuminuria is not evident. In them it is of first importance to exclude inflammation of the urinary tract, stone, tumors, and other non-nephritic causes of albuminuria, the treatment of which is local and surgical. Then the search must be made for a remote focus of infection in tonsils, sinuses about the teeth, in the gall-bladder, in the prostate or seminal vesicles, and any such focus should be eradicated in the hope that from it as a portal of entry has come the infection responsible for the renal damage. Possible toxic causes, especially the inorganic poisons, should be in mind. I have seen albuminuria produced by the therapeutic use of arsenic for instance. In childhood and adolescence, albuminuria without casts and not definitely postural may exist without subsequent evidence of any serious injury to the kidney, and may be more lightly regarded than albuminuria in adult life.

The effect of exercise, cold baths, and so on upon the albuminuria should be studied. I have the records of one patient, who more than thirty years ago, was refused life insurance because of large numbers of hyaline casts in the urine. He came to my father, who discovered that life insurance examinations had always been made in the afternoon, after he had done some lively boxing, and had a cold shower. His urine was perfectly normal at all other times. Twenty-six years afterward he was still free from evidence of chronic nephritis, and, I believe, is still living. Such a patient either needed no advice at all, or to be told to avoid the combination of very active exercise and a cold bath. If exercise produces marked albuminuria with casts it should certainly be reduced.

Apart from wholly temporary albuminuria, however, it is wise for the physician to consider albumin and casts as the evidence of a definite renal lesion, to be watched over long periods of time in the interest of both science and the patient, but not necessarily calling for either a bad prognosis or much interference with the patient's life. Barringer's[4] studies of life insurance statistics show that the persistent presence of granular casts indicates a higher probability of progressive renal disease. Even so, these individuals may enjoy apparently perfect health for ten years or more. It is even more important to watch their blood-pressure than their urine. If this begins to rise, then the development of symptoms is to be looked for. A tendency toward nocturnal polyuria or to fixation of specific gravity is an almost certain danger sign. These point to beginning inability of the kidney to concentrate urea, and therefore connote

[4] The Prognosis of Albuminuria with or without Casts. Arch. Int. Med., 1912, ix, 657–664.

anatomical damage which has reached the stage of seriously compromising the large factor of safety of the kidneys. Until hypertension, nocturnal polyuria, or other symptoms arise, symptomatic treatment is quite unnecessary. Safeguarding treatment is important, but must not go beyond what is of proved efficacy.

Severe physical strain, such as competitive athletics, rough hunting trips and so on, should clearly be avoided. Exposure to cold and wet is also unwise. The wearing of woolen underwear has long been regarded as desirable. Alcoholic and other excesses should naturally be warned against, also the immoderate use of tobacco. The common mild infections, such as tonsillitis, should be much more carefully treated than in normal individuals and the effect on the urine carefully observed.

As to diet, von Noorden[5] has shown that considerable quantities of pepper, mustard, and other condiments are renal irritants. He always held that creatinin was dangerous, and recent work, well summed up and amplified by Myers and Lough,[6] has proved that creatinin retention may be very striking in severe nephritis. Therefore, soups, which are unimportant as sources of energy, and spices may wisely be excluded from the diet. Gourmands should clearly have their excessive appetite restrained, and obese patients should be moderately reduced. If the 'phthalein test is normal I see no reason for a restriction of protein, either qualitatively or quantitatively, below a moderate normal intake. One limitation not immediately necessary, I believe, should be made for the sake of training the patient in case it may become imperative later. Patients who regularly use a large amount of salt with their food—that is the people who habitually put salt on before they have tasted the dish—should be told to reduce their use of added salt at table to foods which come from the kitchen unsalted. Without this training, treatment of subsequent edema in them will meet with serious obstacles. One special category under this heading comprises the diabetics with albuminuria. For them, unless the 'phthalein test shows an excretion below 40 per cent., or there are definite symptoms, such as edema, the treatment is the dietetic treatment of diabetes and the albuminuria should not be allowed to interfere with this.

2. Patients with hypertension, with or without a trace of albumin, and with slight subjective symptoms or none at all. These patients we all recognize at a glance. Since the introduction of blood-pressure measurements into practice they have come into prominence, often, from the stand-point of their comfort, an undesirable prominence. They are usually past middle age. Many of them

[5] Clinical Treatises on the Pathology and Therapy of Disorders of Metabolism and Nutrition—Nephritis, New York, 1903.

[6] The Creatinin of the Blood in Nephritis: Its Diagnostic Value, Arch. Int. Med., 1915, xvi, 536.

are obese, many diabetic. The functional disturbance is so clear-cut, and the anatomical basis in their arterioles so remote from observation, that we usually classify them under the functional category of hypertension. The vast majority certainly have changes in their renal vessels and in the arterioles elsewhere; but the clinical type which I have in mind here does not have renal symptoms. The development of nocturnal polyuria, of severe headaches, especially explosive headaches with vomiting; in patients who have not been subject to migraine, of retinal lesions, or of edema, takes the patient immediately out of this category. Slight cardiac or neurasthenic symptoms are common. Safeguarding treatment is the entire problem of their management. In the first rank must come safeguarding from all avoidable influences which raise blood-pressure in the normal man; next, safeguarding the myocardium and, to a certain extent, the cerebral vessels and the kidneys. The worst hypertensive influence is mental strain, and especially emotional strain. Its avoidance necessarily calls for readjustment of the every-day life for the man in business or for the woman in the home, and the details of this should be worked out with care and sympathy. Distinctly the worst advice is to tell a man of important affairs to give up business completely; but for the manual laborer change of occupation may be imperative. It is of great importance to secure adequate normal sleep. In addition, I believe that the strain of a hard day's work can be greatly reduced by a short break in the middle of the day for absolute rest, or, better yet, for a little exercise, followed by rest. With more marked myocardial symptoms a few days in bed will work wonders, often reducing blood-pressure greatly. Tobacco in excess is clearly a poison both to vessels and to cardiac mechanism. Whether two or three mild cigars a day may be smoked while the patient is sitting quietly after meals must be determined in the individual case. Their effect upon blood-pressure should be observed. If the patient is perfectly miserable without them it may wisely influence the physician. Excessive athletics may be dangerous to both heart and vessels, but I believe that, as a rule, these patients may take more exercise than is usually allowed them—even women who have not previously been accustomed to it. The functional response of the myocardium is the determining factor, and can often be improved by proper exercise. Slight dyspnea on exertion may become less or disappear with gradual training. Mild anginoid pain on exertion, however, calls for great care, and the patient should always stop when it is felt. When exercise cannot be allowed, massage is helpful. The reduction of obesity is a highly important measure. Limitation of diet follows much the same lines as in the preceding class of patients, but physiological economy in nutrition should usually be insisted on, and meals should not be bulky. Moderation in the use of salt, I think, is quite important. The abuse of fluid is clearly dangerous

for them, as von Noorden has insisted. High blood-pressure is no indication of nitrogen retention, as Folin, Denis, and Seymour[7] have shown, and protein should not be restricted merely because of hypertension. Luxus consumption clearly should be, and it is possible that some patients will be, better without meat. On the other hand I am sure that others may be made worse by the loss of appetite that an unpalatable diet produces.

Alcoholic drinks are condemned by von Noorden in these patients. I am not convinced that every patient who has taken wine temperately all his life should be deprived of it absolutely. One should judge by its effects on the circulation. If it causes marked flushing of the face or palpitation it should clearly be avoided; but if it leads to greater enjoyment of meals and to relaxation after it may be permitted. It is needless to say that it should be used sparingly and in dilute form.

Climate has seemed to me not without its influence. The majority of these patients have more symptoms during cold weather, and the combination of cold and high wind taxes the heart maximally. For those who live in the North a winter vacation in a warm climate is desirable. For all of them a long break in their work once or twice a year is most helpful. Turkish baths or other sweating procedures benefit some. Vasodilators should not be used except in emergencies, and aconite, I believe, is worthless.

3. Patients with hypertension and outspoken myocardial insufficiency. This is one of the largest groups to be found in the medical wards of every hospital, and these patients are equally common in private practice. They present primarily the problem of treatment of a circulatory disease. For them both safeguarding and symptomatic treatment are essential. The symptoms demanding treatment in the majority are dyspnea, edema, and the whole picture of cardiac failure with chronic passive congestion of the viscera. A small number have anginoid pain on exertion or severer attacks of angina pectoris. For the latter the essential safeguarding treatment is rest, never permitting enough exercise to produce an attack. Symptomatic treatment consists in the use of vasodilators to cut short or to ward off an attack when exertion must be made. Fresh nitroglycerin tablets dissolved on the tongue and not swallowed have always fulfilled the indications in my experience, and are free from the disagreeable publicity which the breaking of an amyl nitrite pearl entails. Vasodilators have their most important use in these people, who owe Lauder Brunton a great debt of gratitude for the introduction of the nitrites into medicine. Theobromine may be valuable in some cases. It is not necessary for me to go into the treatment of angina in further detail.

[7] The Non-protein Nitrogenous Constituents of the Blood in Chronic Vascular Nephritis (Arteriosclerosis) as Influenced by the Level of Protein Metabolism, Arch. Int. Med., 1913, xiii, 224.

The patients with ordinary myocardial failure do not present a simple problem of circulatory therapeutics. Their study by the nephritic test meal, originally advocated by Schlayer and Hedinger, and which Mosenthal[8] has adapted and amplified with such excellent results in our clinic, has shown the importance of the special functional changes, depending upon chronic passive congestion of the kidney in retaining salt, and thus in producing at least the edema if not other symptoms of the disease. Every case of this type should, I believe, be given such a test, and should have a phenolsulphonephthalein test as a preliminary to treatment. If, in addition, the blood urea and the Ambard coefficient can be determined, very valuable information may be gained. The 'phthalein output is usually low, often under 30 per cent., sometimes minimal. If normal, or nearly so, and the test meal shows no lowering of the nitrogen concentration in the urine and no marked nitrogen lag, then it is rarely necessary to determine the blood nitrogen. Only in moribund patients can important retention exist. It is also essential to recognize the presence or absence of fibrillation of the auricles as a guide to the use of digitalis. Clark's[9] study of venous pressure in our wards, using Hooker's simple method, has also given us valuable indications of the need for digitalis.

All these patients require rest in bed, or in a chair if they are orthopneic, as the essential safeguarding treatment for the heart. Those with auricular fibrillation must receive effective digitalis treatment. Choice of the preparation and the method of administration, as between strophanthin intravenously or intramuscularly, infusion or tincture of digitalis, the powdered leaf of digipuratum, being determined by the details of the case and the habits of the physician. Those without auricular fibrillation, but with marked edema and a congested liver, should, I believe, also be placed on digitalis. Many of them will respond as well as the fibrillating cases; others will not. Toxic effects must be watched for and heeded, as some patients with regular rhythm are made worse by digitalis. If it does not succeed alone with proper diet, then one of the caffein diuretics—theocin, about twelve grains a day, or diuretin, about forty grains, in divided doses—should be given not oftener than every other day. It is very important to have the fluid intake and urine output accurately measured, and it is helpful to have the daily weight recorded. Diuresis from digitalis by the ordinary administration by mouth should not be expected before forty-eight hours. The diuresis of the caffein group of drugs, however, should be observed on the chart of the day of administration, and may

[8] Renal Function as Measured by the Elimination of Fluids, Salt, and Nitrogen, and the Specific Gravity of the Urine, Arch. Int. Med., 1915, xvi, 733.

[9] A Study of the Diagnostic and Prognostic Significance of Venous Pressure Observations in Cardiac Disease, Arch. Int. Med., 1915, xvi, 587.

then persist for one or two days longer. The next doses should be given when the diuresis ceases.

NEPHRITIC TEST DIET.

For..... Date.....

All food is to be *salt-free* food from the diet kitchen.

Salt for each meal will be furnished in weighed amounts.

All food or fluid not taken must be weighed or measured after meals and charted in the spaces below.

Allow no food or fluid of any kind except at meal times.

Note any mishaps or irregularities that occur in giving the diet or collecting the specimens.

Breakfast, 8 A.M.:

Boiled oatmeal, 100 gms.	
Sugar, 1 to 2 teaspoonfuls..	
Milk, 30 c.c.	
Two slices bread (30 gms. each)	
Butter, 20 gms.	
Coffee, 160 c.c.	
Sugar, 1 teaspoonful	−200 c.c.
Milk, 40 c.c.	
Milk, 200 c.c.	
Water, 200 c.c.	

Dinner, 12 Noon:

Meat soup, 180 c.c.	
Beefsteak, 100 gms..	
Potato (baked, mashed or boiled) 130 gms.	
Green vegetables as desired	
Two slices bread (30 gms. each)	
Butter, 20 gms.	
Tea, 180 c.c.	
Sugar, 1 teaspoonful	−200 c.c.
Milk, 20 c.c.	
Water, 250 c.c.	
Pudding (tapioca or rice), 110 gms.	

Supper, 5 P.M.:

Two eggs cooked in any style	
Two slices bread (30 gms. each)	
Butter, 20 gms.	
Tea, 180 c.c.	
Sugar, 1 teaspoonful	−200 c.c.
Milk, 20 c.c.	
Fruit (stewed or fresh), 1 portion.	
Water, 300 c.c.	

8 A.M. No food or fluid is to be given during the night or until 8 o'clock the next morning (after voiding), when the regular diet is resumed.

Patient is to empty bladder at 8 A.M., and at the end of each period, as indicated below. The specimens are to be collected for the following periods in properly labeled bottles, to be furnished by the chemical division of the medical clinic: 8 A.M. to 10 A.M.; 10 A.M. to 12 N.; 12 N. to 2 P.M.; 2 P.M. to 4 P.M.; 4 P.M. to 6 P.M.; 6 P.M. to 8 P.M.; 8 P.M. to 8 A.M.

Specimens are to be left in the ward until called for at 8.30 A.M. by an attendant from the chemical laboratory.

REPORT ON NEPHRITIC TEST MEAL.

Name..... Date.....

Time of day.	Cubic centimeters	Specific gravity.	NaCl. Per cent.	NaCl. Grams.	N. Per cent.	N. Grams.	Time and c.c. of fluid intake.
8 to 10	153	1.016	1.32	2.02	.89	1.26	
10 to 12	156	1.019	1.25	1.95	.74	1.15	
12 to 2	194	1.012	.64	1.24	.59	1.14	
2 to 4	260	1.014	.77	2.00	.56	1.46	
4 to 6	114	1.020	.99	1.13	.95	1.08	
6 to 8	238	1.010	.43	1.02	.52	1.23	
Total day	1115	.....	....	9.36	....	7.32	
Night, 8 to 8	375	1.020	.63	2.36	1.23	4.61	
Total 24 hours	1490	.....	....	11.72	....	11.93	
Intake	1760	.....	....	8.5	....	13.4	
Balance	+270	.....	....	−3.22	....	+1.47	

Impression. Normal reaction to the nephritic test meal. Note the variations occurring in the fluid output and the specific gravity, which are in inverse ratio; the night urine, which is small in amount and shows a high specific gravity and a high percentage of nitrogen, and the approximately normal output of water, salt, and nitrogen.

Regulation of the diet is one of the most essential features of treatment. Thanks to our functional studies we can now base this upon the individual requirements of the case, not upon so-called general principles. The three factors to be considered are the fluid, the salt, and the nitrogen intakes. Practically all of these patients require limitation of their fluid intake, the degree of limitation depending upon the observed lag in water output and the amount of edema. It is scarcely possible, however, to discuss the water exchanges separately from the salt, since in these patients they are concurrent. The most distinctive result of the test meal in myocardial insufficiency, without renal involvement other than chronic passive congestion, is a low-water output with fairly high specific gravity, nearly always 1020, extremely low salt concentration and total output, and, in contrast, a normal nitrogen excretion brought about by the high concentration of this substance in the urine. The greater the degree of accompanying contraction of the kidney the more the specific gravity tends to be fixed and at a low level, nocturnal polyuria to become marked, and the concentration of the nitrogen, especially in the night urine, to fall far below the normal. With any of these features in evidence it is necessary to further test the functional capacity of the kidney for nitrogen by the determination of the blood urea and, best, by the comparison of this with the urinary urea in the Ambard formula. Whether this is better expressed, as in the recent admirable work of McLean, of the Rockefeller Institute, as an index of urinary

excretion, on the basis of a normal standard of reference of 100, or by Ambard's coefficient, the normal value for which is 0.06 to perhaps 0.09, is not clear to me. It is desirable that we should not have to burden our minds with any unnecessary arbitrary numerical values. Since Ambard's coefficient is already widely used the desirability of another set of values for expressing the same functional test should be clearly demonstrated before being adopted. The new values have mnemonic simplicity in that 100 is ideal perfection and the calculation is much simplified, but the range of normal values, from 80 to over 200, is rather wide.

A high Ambard or a falling index of urea excretion, or blood nitrogen above the normal, indicates the need for limitation of the protein intake. Ambard considers the normal constant 0.07. Unpublished observations by Lewis, in our clinic, show that 0.09 is more nearly the upper normal limit. There is considerable difference of opinion as to the figure for urea which may be found in the blood of healthy persons, but our experience coincides with McLean's[10] that 50 mgs. per 100 c.c. is possible with very high protein diet. Apart from this, 40 mgs. should never be exceeded. The urea nitrogen is practically one-half of this. The total non-protein nitrogen should rarely pass 40 mgs. per 100 c.c. under any circumstances. The small range found by Folin and Denis[11] in absolutely healthy individuals, 22 to 26 mgs., is too ideal a standard to apply to patients. The practical means for accomplishing this limitation vary from a low protein diet, which can never be an exclusive milk diet, to the introduction of short periods of nitrogen starvation in the worst cases. In such periods carbohydrate food should be given freely to spare protein. A satisfactory low-protein diet devised by Mosenthal for use in our wards follows:

THE JOHNS HOPKINS HOSPITAL.

LOW PROTEIN DIET.

Breakfast:

Sherry, 30 c.c.
Baked apple, stewed prunes, orange.
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch).
Cream, 15 c.c.

Dinner:

Sherry, 30 c.c.
Potato, baked or mashed.
String beans, cabbage, carrots, lettuce, onions, tomatoes, cucumber pickles.
Fruit cornstarch pudding, fruit tapioca pudding.

Supper:

Same as dinner. (Salt, sugar and butter may be used as desired, and need not be weighed.)

[10] The Numerical Laws Governing the Rate of Excretion of Urea and Chlorides in Man, Jour. Exp. Med., 1915, xxii, 212, No. 2; 1915, xxii, No. 3.

[11] Protein Metabolism from the Standpoint of Blood and Tissue Analysis—Sixth Paper, Jour. Biol. Chem., 1913, xiv, No. 1.

NITROGEN CONTENT OF FOODS USED IN LOW PROTEIN DIET.

Article of food.	Percentage of nitrogen.
Cream	0.41
Cereal:	
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch)	.13
Fruit:	
Baked apple	.04
Orange	.16
Stewed prunes	.14
Vegetables:	
Cabbage	.16
Carrots	.10
Lettuce	.24
Onions	.17
Cucumber pickle	.10
Baked potato	.48
Mashed potato	.40
String beans	.23
Tomatoes	.23
Desserts:	
Blackberry cornstarch pudding	.05
Prune cornstarch pudding	.07
Apple tapioca pudding	.02
Peach tapioca pudding	.06

Failure to eliminate salt makes essential the reduction of the salt intake to a figure below the twenty-four-hour output. Where much edema exists a rigorous salt-poor diet containing less than 3 grams, if possible getting the amount down to 1 gram, is most desirable at the start. Since these patients with myocardial insufficiency and marked edema require strict limitation of fluids as well the Karell diet is ideal. As is known, this consists of 800 c.c. of milk in the twenty-four hours as the only food or fluid allowed. Karell was a Russian physician who introduced this diet as a somewhat empirical cure for dropsy fifty years ago. We now possess entire theoretical justification for its use as a rational measure of safeguarding treatment, which is also highly effective in the cure of a most distressing symptom. It has the great virtue of simplicity. It can be carried out in households where an accurate salt-poor diet of any other kind would be impossible. Disappearance of edema usually begins after two or three days in this myocardial group of patients, and is little short of magical. When diuresis is abundant and the dropsy disappearing rapidly the amount of milk can be gradually increased up to 1500 c.c., and then other appropriate foods gradually added. It is desirable to determine the degree of restoration of the power of the kidney to excrete salt before allowing return to a full diet. All such patients should be warned against the abuse of salt for the future, and must never take large volumes of fluid or bulky meals. I think tobacco should be forbidden, but I am not sure that a little alcohol is harmful.

After recovery from the urgent symptoms the return to physical activity must be by very gradual stages and carefully supervised. Massage, resistance movements, and hydrotherapeutic procedures are all helpful here. Fibrillating cases must, if they show any tendency to a rate above the normal, take small doses of digitalis more or less constantly, the dosage to be determined by observation.

4. General edema without notable myocardial insufficiency the prominent symptom. This group of patients is much smaller than the preceding, and is met more frequently in hospital wards than in private practice. A considerable proportion of these dropsical patients have a subacute or chronic diffuse nephritis—that is a true inflammatory lesion of the kidney involving glomeruli, tubules, and interstitial tissue. This was what Dr. Delafield called chronic diffuse nephritis with exudation. Their urine is highly albuminous, and contains casts of all kinds. The common name given this type of disease, chronic parenchymatous nephritis, is altogether a misnomer. A number of them, under careful treatment, prove to be cases of very protracted acute nephritis, and will eventually make a functional recovery. Others develop increasing renal insufficiency with uremia and enter the next group, which I shall describe later. A few patients of this type, with the most obstinate edema and low blood-pressure, prove at autopsy to have amyloid kidneys. Still others are examples of a degenerative lesion of the tubular epithelium, not an inflammatory process. The cause of this we do not know, but its similarity to the effects of certain inorganic poisons makes a chronic intoxication plausible. The pregnancy kidney is a special example of this type. Following Friedrich Müller, Volhard and Fahr[12] in their recent book use the term nephrosis to describe these non-inflammatory cases. Their diagnostic criteria are the absence of blood elements in the urine and the absence of a rise in blood-pressure. Those who are interested in the pathology of renal disease I would refer to this admirable anatomical and clinical monograph. Widal,[13] on the other hand, adopts a purely functional classification. While I do not believe the functional disturbances permit of so clean-cut a subdivision of renal disease as he makes, and should be personally dissatisfied with a diagnosis which did not rest upon an anatomical basis, still this particular type has so predominant a disturbance of the salt and water excretion as to justify his name salt-retention nephritis. Certainly for treatment this is the essential feature to recognize, and Widal and Javal's[14] work on the effects of withholding and feeding salt in such cases has been one of the great recent advances in practical therapeutics. When tested, either by the nephritic

[12] Die Brightsche Nierenkrankheit, Berlin, Julius Springer, 1914.

[13] Les Grands Syndromes du Mal de Bright, Jour. med. français, Paris, 1911, v, 18–33.

[14] La cure de déchloruration, Paris, J. & B. Baillière, 1906.

test meal or by the addition to a constant diet of an added ten grams of salt, these patients all show a striking failure to excrete sodium chloride. The salt concentration in the urine is often as low as 0.1 per cent., and the daily output not over one gram for long periods. With this the amount of urine is naturally very small and the retained water and salt accumulate in the subcutaneous tissues or serous sacs. Whether in all these cases the power of the kidney to excrete salt is primarily affected is very doubtful. It is highly probable that in many an increased affinity of the tissues for water, is equally important with the state of the kidney. For practical purposes of treatment it makes no difference. Salt and water are being retained. The 'phthalein test and the ability to excrete nitrogen may show unimpaired kidney function in every other respect. The potassium iodide test of Schlayer shows tremendous delay in excretion, but to me has no practical significance. The important point to determine is the degree of impairment of the ability to excrete water and salt. One patient may put out five grams of sodium chloride a day, another only one gram. For the first a diet containing three grams will lead to disappearance of the edema; for the other the most rigorous salt-poor diet will be without effect. Treatment should always begin by a period of very low salt and water intake to promote rapid absorption of the dropsical effusions. When this has been accomplished the response to increased water intake should first be tested and fluid pushed as fast as it can be excreted. The response to added salt should later be tested from time to time and the intake gradually increased, with care to keep always below the tolerated amount. Bed is desirable until normal function is restored. The problem of further treatment is that of the convalescence from acute nephritis. Local foci of infection should be looked for and the patient safeguarded from exposure, strain, and all injurious surroundings.

Patients with very low salt outputs and obstinate edema require accessory dehydrating measures, of which sweat baths have, in my experience, been the most effective. Purging may be of some value. In one patient hot packs were promptly followed by diuresis, the absorption of an obstinate edema of nineteen months' standing, and a prompt rise in the salt concentration of the urine. Retention with recurrence of edema was immediate upon cessation of the packs, and again disappeared upon their resumption. Such an influence is hard to explain, but suggests an alteration in the kidney circulation, acting upon the lesion itself. Borderline cases between this group and the preceding require a suitable combination of cardiac therapy with that just outlined.

5. Advanced renal insufficiency, uremic symptoms superimposed upon one of the foregoing types. We all recognize this as the classical picture of the end-stage of chronic Bright's disease. It is much easier to recognize than to define. Uremia can best be considered

with Ascoli as the varied disturbances, chiefly of the central nervous system, seen clinically in association with disease of the kidney or obstruction of the urinary tract and not dependent upon gross anatomical lesions of the brain. The differentiation of the severe headache of uremia and that due to cerebral vascular disease or of a uremic from an organic coma or hemiplegia may be very difficult. Lumbar puncture sometimes gives the clue, and should be resorted to. The gradually developing uremia which I have in mind here, however, with increasing headache, attacks of vomiting, respiratory disturbance, irritability, delirium, or drowsiness, gradually passing into terminal coma, scarcely permits of confusion, except with similar toxic states, as in the end-stages of liver disease. Changes in the optic nerve or retina are practically always present in true uremia, and the functional tests show what we may well consider as quantitative renal insufficiency. The test meal can be safely used only in the early stages, and then should frequently have its protein content reduced. It will show nocturnal polyuria, fixation of the specific gravity at a fairly constant, sometimes an absolutely constant, level, which is low in proportion to the severity of the renal insufficiency. It indicates inability of the kidney to excrete the normal constituents in anything but low concentration. The functional picture is constant in advanced contracted kidney, but may vary from week to week in diffuse nephritis. In our experience both nitrogen and NaCl concentrations have been equally reduced. Frothingham and Smillie[15] have found this also. This makes Widal's distinction between nitrogen-retention nephritis and salt-retention nephritis invalid. Sodium chloride excretion may be affected as an isolated functional disturbance, but nitrogen excretion seems only to be affected in quantitative renal insufficiency in company with all of the other functions except that of water excretion, which may remain intact. This NaCl retention does not necessarily lead to edema. The patients often have great thirst, considerable polyuria, and loss of weight, with dryness of the skin and tissues. This dry salt retention emphasized by the French school is of much theoretical interest. The 'phthalein test is of diagnostic, prognostic, and therapeutic importance. The excretion is diminished in proportion to the degree of renal insufficiency, and, as a rule, parallels closely the Ambard coefficient and the degree of increase of the non-protein nitrogen of the blood. When blood analyses are not possible it is the best practical measure of the probable degree of nitrogen retention, so-called. Agnew[16] has shown that in experimental renal lesions the blood nitrogen remains normal when the 'phthalein output is over 40 per cent. for the

[15] A Study of Different Nitrogenous Diets in Chronic Nephritis, Arch. of Inter. Med., 1915, xv, 204.

[16] Comparative Study of Phenolsulphonephthalein Elimination and the Incoagulable Nitrogen of the Blood in Cardiorenal Diseases, Arch. Int. Med., 1913, xiii, 485.

two hours. The most advanced cases excrete mere traces. All subsequent observers have confirmed the importance of Rowntree and Geraghty's[17] test in the prognosis and management of these cases.

The Ambard[18] coefficient is always raised and is unquestionably the most accurate measure of the degree of impairment of the urea excretion, though data in a large number of cases are not yet available. Widal's figures for blood urea remain the nearest approach to a prognostic standard if one remembers that they were obtained by the hypobromite method and represent more nearly total non-protein nitrogen. With 50 to 100 mgs. per 100 c.c. a long survival is possible, though prognosis must be guarded. With more than 100 mgs. no case lived over two years nor over one year if 200 mgs. were found. Over 500 mgs. were only found just before death. Certainly, in our experience, no case with over 300 mgs. of total non-protein nitrogen per 100 c.c. or an Ambard above 0.4 lived many weeks. On the other hand, Foster[19] has shown that low blood nitrogen does not insure a good prognosis.

Treatment of the severest renal insufficiency is purely symptomatic and not a cheerful duty. The distressing paroxysms of dyspnea and of Cheyne-Stokes breathing usually demand special relief. The low alveolar CO_2 shows acidosis, but alkali has not relieved the symptom. For many patients morphin alone is effective, but it is a two-edged sword—it occasionally precipitates the rapid onset of anuria with coma, and once begun has to be used in increasing doses. Nothing requires more judgment on the part of the physician. Chloral hydrate in 5 or 10 grain doses, alone or combined with moderate doses of bromides, is sometimes very effective and should always be given a trial. Insomnia is commonly bound up with the onset of dyspnea on first lying down or with the recurrence of dyspneic paroxysms through the night. One serious practical mistake made by many physicians is to insist on these sufferers going to bed. Instead they should be encouraged to sleep in a chair until one is sure that he can promise them a real sleep in bed. Bed soon acquires for them a mental association with respiratory distress, and acts by suggestion as well as directly. The breaking up of this suggestion through a few good nights in a chair may make possible the return to restful sleep in bed. In some of the milder cases I have had great success by the use of a vasodilator just before retiring. For this purpose I prefer sodium nitrite, the effects of which are more lasting. It should be given about fifteen minutes before bedtime.

The gastro-intestinal disturbances, I believe, are of central nervous origin or eliminative. I feel sure that water and NaCl

[17] An Experimental and Clinical Study of the Functional Activity of the Kidney by Means of Phenolsulphonephthalein, Jour. Phar. and Exp. Ther., 1910, i, 579.
[18] Physiologie Normale et Pathologique des Reins, 1914, Paris, F. Gittler.
[19] Functional Test of the Kidney in Uremia, Arch. Int. Med., 1913, xii, 452.

are removed by vomiting and perhaps a little of the retained nitrogen. Treatment is apt to be very ineffectual. Lavage of the stomach and of the bowel are worth trying, but for the most part it is a problem in the use of general sedatives.

Diet is usually reduced to a minimum by the patient, for anorexia is the rule. In the severer degrees of insufficiency only starvation can hinder the nitrogen accumulation, and nothing prevents the terminal rise in blood nitrogen. In the early cases a very low nitrogen diet is strictly indicated with nitrogen starvation on days of severe symptoms, giving as much carbohydrate as possible. We have had a few remarkable improvements from this treatment. More frequently it is merely a choice of evils. The amount of fluid should depend upon the urinary output, and should be limited only by this or by the occurrence of edema. Vomiting, of course, will entail self-limitation. Of direct measures to reduce the retention of poisons, bleeding takes first place, but bleeding increases the anemia, which is so apt to be a feature of the intoxication. In a few recent cases repeated bleedings with consecutive transfusion have produced definite symptomatic improvement, and at times seemed to hold the blood nitrogen down. We have hoped that Abel's[20] operation of plasmapheresis might prove useful in these cases. It consists in bleeding into a non-clotting solution, separation of plasma and corpuscles by centrifugation, removal of the plasma, and reinjection of the corpuscles suspended in Locke's solution. One case done with hirudin, which was quite harmless to Abel's dogs, had a violent febrile reaction with shock, but recovered later and was considerably improved. We are cautiously testing the procedure further, using citrate, but have no successes to report as yet.

Bleeding has its greatest value in the case of sudden convulsive seizures. These so-called acute uremic or eclamptic convulsions have, in my experience, occurred in patients who did not have advanced renal insufficiency with marked nitrogen retention. The removal of at least 500 or 600 c.c. of blood is regularly indicated and recovery is common. I have known a number of such patients to live for several years after severe convulsions. I believe that the causation of these convulsions is analogous to that of the convulsions which occasionally mark the onset of acute scarlatinal nephritis, and has nothing in common with the causation of the chronic uremia which accompanies advanced renal insufficiency. Many are undoubtedly due to cerebral vascular disease. Sweating occasionally seems to benefit the patient.

The most important treatment in uremic cases is of associated myocardial insufficiency, when it exists. The superposition of chronic passive congestion on moderately damaged kidneys may

[20] Plasma Removal with Return of Corpuscles (Plasmapheresis), Jour. Phar. and Exp. Ther., 1913, v, 625.

precipitate severe renal insufficiency. In other words a person who has lost the part of his reserve kidney tissue which constitutes the factor of safety, and is, roughly, about two-thirds of the total, may be thrown into the severest renal insufficiency by purely functional disturbance of the kidney circulation, as he may also be by the occurrence of an acute intoxication or infection leading to fresh anatomical lesions of an acute type. The prognosis when myocardial insufficiency is marked is always much better, because the element of functional disturbance may be recovered from under appropriate treatment of the heart, while gradually increasing renal insufficiency, due to progressive destruction of the kidney tissue, must have an absolutely hopeless outlook.

Of equal importance, but less generally appreciated, is the urgent necessity for the treatment of any associated obstruction of the urinary tract. Back pressure from an enlarged prostate with even moderate residual urine, combined with an only slightly damaged kidney, may rapidly lead to severe renal insufficiency, with uremia. The recent work of the genito-urinary surgeons in this field should be familiar to all medical men. The extent of the damage to function is demonstrated by the phenolsulphonephthalein test, as Rowntree and Geraghty[21] early showed in patients from Dr. Young's urological clinic, and Mosenthal has found the same indications in the study of such patients with his test meal. I have personally seen what was apparently advanced contracted kidney, with extreme hypertension and serious uremic symptoms, in a man, aged seventy-six years, transformed to a comparatively benign arteriosclerosis of the kidney, with hypertension, after the relief of back pressure by removal of the prostate. The patient was restored to practically ordinary health and working ability for a man of his years. In elderly men especially the possibility that urinary obstruction is the chief cause and renal disease the accessory cause for renal symptoms should never be out of mind. Pyelitis and pyelonephritis may produce similar pictures. Modern surgery in such conditions may make medical management superfluous.

A final word as to the possibility of surgical treatment in uncomplicated nephritis. Reginald Harrison first proposed this nineteen years ago, calling attention to the possibility of mechanical damage to the kidney circulation by pressure of the unyielding fibrous capsule upon a swollen edematous kidney. He proposed the relief of this mechanical factor by incision of the capsule. Five years afterward the late Dr. Edebohls, of New York, proposed to restore a damaged kidney circulation by decapsulation and the production of a collateral circulation between the cortex of the kidney and the surrounding tissues, and somewhat later Sippel advocated decap-

[21] The 'Phthalein Test: An Experimental and Clinical Study of Phenolsulphonephthalein in Relation to Renal Function in Health and Disease, Arch. Int. Med., 1912, ix, 284.

sulation of the kidney for puerperal eclampsia. The whole subject has been recently well reviewed by Ruge in the *Ergebnisse der Chirurgie und Orthopedie*.[22] He makes it clear, in spite of considerable contradiction in the interpretation of the results obtained, that we medical men should more carefully consider the possibility of improvement by nephrotomy or decapsulation in certain cases both of acute and chronic nephritis which do not respond satisfactorily to our usual measures. The need for better methods of treatment is plain. The field is peculiarly one for coöperative studies. I have personally witnessed a number of failures, but two cases stand out in my experience which I would record in this connection:

Both had persistent edema, hypertension, retinal lesions, and uremic symptoms extending over months, under my observation, in St. Luke's Hospital, New York. Both made an eventual complete functional recovery, being left only with albumin and casts in the urine and a moderate elevation of blood-pressure. Even the retinal lesions disappeared and both were well seven years later Both had decapsulation performed. In one the improvement followed so closely as to suggest that the operation was its cause. The other had been decapsulated before she came to us, and improvement was so long delayed as to make the relation wholly improbable. I have seen no other recoveries after decapsulation in patients with severe renal insufficiency. I am inclined to believe that these two patients had a protracted subacute diffuse nephritis, and that the inflammatory process subsided without assignable cause, though possibly some remote focus of infection ceased to act as a portal of entry. In the first I feel sure, however, that the operation, probably by relieving tension within the capsule and improving the blood flow through the kidney, at least hastened the recovery. One would not anticipate any advantage from operation on advanced contracted kidneys.

In conclusion, may I emphasize the obvious summing up of the whole matter. Improved methods of investigation now permit of the much more accurate analysis of the various factors entering into the production of the complicated symptomatic pictures of chronic renal disease. Such analysis makes possible the more exact adjustment of treatment to the needs of the individual case and the relief of the patient from burdensome and unnecessary restrictions. In spite of all this it brings us not one whit nearer the real goal of treatment, prevention, or cure of the disease. If we ever achieve this it will be through new knowledge of the causes of these obscure but frequent affections, and every attempt to approach this problem from a new view-point should be enthusiastically welcomed by every medical man.

[22] Ueber den derseitigen Stand einiger Nephritisfragen und der Nephritischirurgie, loc. cit., 1913, vi, 565; see also Jour. Am. Med. Assn., October 2, 1915, lxv, 1188.

THE RELATION OF PROGNOSTIC FACTORS TO TREATMENT IN DIABETES MELLITUS.

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We are not in the habit of considering those factors which influence prognosis as intimately related to the problem of therapeutics. The reason we do not do so is because we customarily think in the terms of acute disease. The necessity of considering prognostic factors therapeutically is self-evident. When a man suffering from chronic renal disease is advised to seek a mild winter climate the physician is trying to avoid the danger to his patient from pneumonia. He considers a prognostic factor as a problem in preventive therapeutics. He may not ponder, but he knows that of individuals with chronic disease only a minority die of that disease, the majority, weakened and undermined in health, die of acute superimposed infections or of complications. The apt formula of a famous American physician on how to live to old age is pat: "Acquire a chronic disease and take care of yourself."

If, then, we are to advise intelligently patients with maladies such as chronic nephritis, and diabetes we must form a very clear estimate in each case as to just what the dangers are which menace his existence. This is necessary in order to carry out the prime endeavor of prolonging life—and it is no less requisite that we consider these factors in the means adopted to ameliorate the symptoms of the disease. The two goals of therapeutic endeavor, prolongation of life and the amelioration of symptoms, are secured but seldom by a change in the individual; not infrequently by a change in the environmental demand. Therapy directed to etiological factors is at present almost unknown in the realm of chronic disease.

These principles find no better example than in the treatment of patients with diabetes mellitus. With this disease, perhaps, more than with any other, the afflicted is out of joint with his environment; he can no longer eat or work with his brother man. We are apt not to think of it, but the condition is appalling. Every single human privilege is walled off by an adaptation to a narrowed function.

Now what are the dangers which beset the existence of the patient with diabetes? Numerically, infections take first rank and account, directly or indirectly, by precipitating coma for over 78 per cent. of the deaths. Elsewhere[1] I have called attention to the frequency of surgical infections, but I do not wish at present to limit my

[1] Diabetes Mellitus, Philadelphia, 1915.

remarks to any one type. Even a slight cold becomes a very serious complication with a diabetic child; tonsillitis that would hardly confine a healthy man to the house has sent many diabetics to the grave. Tuberculosis is proverbially common among diabetics seen in hospital practice, less so among the well-to-do. Pneumonia, in my experience, has been invariably fatal, often because it precipitates acidosis and coma. Since these dangers which kill the majority of diabetics menace all alike, any mode of treatment which disregards these prognostic factors is lacking in foresight. Once contracted, infections are difficult in any case to combat, and often the fight is hopeless; the only safety is in keeping the patient in some condition approximating to normal vigor, so that infective agents find a less fertile soil. This principle concerning infections, as related to bodily vigor, is established, and finds no exception in the realm of chronic disease. Disregard of one ultimate aim of therapy in diabetes—namely, an approach toward a healthy state of resistance to infectious disease, so often leads to calamity that I am frankly pessimistic for that group of cases that can attain and preserve a sugar-free urine only at the expense of nutrition. With a sufficient number of cases it will, I think, be manifest that one danger has been exchanged for another.

There is no question in my opinion that the *average* diabetic not only has more comfort and sense of well-being when his urine contains no sugar, but that his actual resistance to infection is higher. I refer now to cases in middle life in which a severe glycosuria is not complicated by acidosis and in which undernutrition and loss of strength are the striking features. The majority of these cases regain strength and energy after the glycosuria is controlled. With others the diet which controls the glycosuria necessitates that the patient remain some 20 per cent. under normal weight, while with a diet that holds him but 10 per cent. under weight he has about fifteen grams of sugar daily in the urine. Now which is the preferable condition? Neunyn said that he did not know, and I doubt if we do at present. Again, exercise benefits the majority, but some patients have slight rises in temperature after exercise, and without the exercise the tolerance is too low for safety. It seems to me that here we have questions not related to our ideals of treatment but intimately concerned with the future of our patient, and they are best decided by remembering from what direction danger approaches.

As to whether a sugar-free urine indicates a state of affairs in the body economy which may be spoken of as holding the diabetic tendency in control, I have some doubts. There are facts which speak against it, as, for example, the frequency of pathological organic changes which develop after long periods during which the diabetes is apparently under full control. I refer to renal disease in the younger patients and nerve lesions in all. As a matter of fact,

we are not able to effect the end we strive for. As proof that we are not overtaxing the body's powers to handle sugar, we customarily accept the fact that the urine does not contain glucose. But this is not the criterion. The real criterion is the percentage of blood sugar; and with any cases other than the mild ones the blood sugar remains above normal and can be reduced to normal only during periods of excessively low diet or absolute fasting. In other words, there is a considerable margin between the maximal normal (0.14 per cent.) of blood sugar concentration and the *threshold of renal permeability* (0.16 to 0.17 per cent.); constant hyperglycemia means a continuation of an abnormal state. We can successfully remove the overload, it is true, when we reduce the blood sugar from 0.35 or 0.45 per cent. down to 0.16 or 0.17 per cent., and with the majority of patients that reduction effects a wonderful change in general health. But 0.16 per cent. is not a normal blood sugar. The blood then and not the urine is the measure of whether the means we employ are suitable. With some of the severest and most hopeless cases that have come under my observation the urine contained no sugar at a time when the blood sugar, due to a concomitant kidney disease, was as much as three times the normal. Evidently the urine may mean nothing as to the diabetic state.

To excessive hyperglycemia is in my opinion to be assigned a large degree of impairment of function, and this idea I can best make clear by an analogy drawn from chronic nephritis. It is a common observation that with these cases of chronic renal disease at periods before treatment, all the tests and the metabolism studies may indicate a hopeless degree of renal damage, the urea of the blood may be very high and the 'phthalein excretion reduced to traces. After an appropriate regimen the same tests indicate a clear-cut increase in the ability of the kidney to perform its function. This phenomenon we may style a depression of function due to the overload. With diabetes the state of affairs is not very different. At times when there is marked hyperglycemia the tolerance appears *nil;* after a couple of months of treatment, when the blood sugar is reduced to only a little over normal, there is often a surprising ability to use carbohydrate. For this reason I think it is impossible to tell in advance whether any given case is mild or severe. Many that seem severe in the beginning, even with considerable acidosis, prove after a year to be only mild. But this is true *only when* the disease is *not of long duration.* With cases in which the indications are that a year or two at most have passed before treatment is commenced, my results have been very encouraging when the patients could do what their disease demanded. For this reason I shall divide my cases into two groups, early and advanced. The severity of the acidosis or glycosuria with these cases in the beginning was no criterion of the actual conditions, and this is adequately demonstrated by cases that were infused at the commencement

of treatment because of incipient coma. The history with these cases indicated about a year's duration of the diabetes. Some of these individuals are now using, on five days of the week, unrestricted amounts of starch without resultant glycosuria. One of them has a normal blood sugar unless the routine vegetable day be omitted for several weeks. All are young, under thirty-five years, and all are up to normal weight and vigor. These and other cases I have studied illustrate the difficulty stated by Joslin in differentiating mild from severe diabetes. I know an old gentleman who was a severe diabetic at the age of twenty-two years. He is now nearly seventy and has had no glycosuria for forty years. He was a patient of the elder Shattuck. In fact, I question whether the terms mean just what we wish to express when we speak of young patients with glycosuria and severe acidosis. Should we not rather say early and advanced? (The older cases are in a class by themselves in which acidosis is but seldom of moment, even when of considerable degree, as Neunyn pointed out.) My experience of the last five years has been that with young adults who came under observation early after the disease was recognized, all have secured sugar-free urines, notwithstanding severe acidosis at the start, and all who followed advice have recovered a considerable degree of tolerance for carbohydrate, much above what it was in the beginning of treatment.

Concerning the cases of young adults, four to five years of age, who were observed first when the disease was of some years' duration —that is, advanced cases—the results have not been encouraging even when, as often happened, on account of but slight acidosis, it appeared in the beginning that the task was much easier than with some of the early cases. The glycosuria may be easily controlled, but the blood sugar is difficult to reduce to normal, and it remains normal only under the most restricted conditions. As a rule, the tolerance secured is too meager to preserve health over long periods. My observation indicates that with this group those patients who have adhered to diet have died of complications and infections wherein coma occurred only as a sequel to acute disease, *i. e.*, pneumonia or la grippe. Of those who have not been so rigidly dieted or who have not observed diet with due care the majority have died in coma. The period of life in both groups averages over two years from the beginning of treatment. An estimate of value of treatment as measured in years of life can be discovered only by a very large number of cases observed for years. The point is that with advanced cases in young persons the results are discouraging even when the disease is apparently under control. And I might add here that this statement applies also to diabetic children. Cases now living that have been for several years ideal so far as absence of glycosuria indicates, are under height, under nourished, and altogether most pathetic.

One interpretation of these facts as I understand them is this: That with *early* cases we can expect much from treatment. Vigilant control of the diet so that glycosuria is absent and the blood sugar down to nearly normal is justified, since with time tolerance increases. Even a dangerous degree of acidosis does not necessarily frustrate this design. This interpretation rests on the hypothesis that I have stated earlier in the paper—namely, that the hyperglycemia itself induces pathological function. The alternative interpretation is that these early cases that are now doing well will eventually deteriorate and become the typical advanced case. It will take years to decide this point, but against this contention is the increased tolerance for carbohydrates observed as years go by. It is to be remembered, however, that some young adults with severe diabetes and considerable acidosis live six to ten years under the less stringent methods which aim only to keep sugar excretion low, but never abolish it completely. But it is my belief that with those cases in which the diagnosis is made early much can be accomplished by vigorous treatment. It matters not whether the blood sugar be reduced by the rapid method of complete fasting or by the slower method of periodic fasts; *the end that must be attained is a sugar-free urine, blood sugar as near normal as possible, and an absence of acidosis.*

The chief danger lies in the after period, when because the urine is so persistently normal, patients, and even physicians, are led to doubt the necessity of the diet, with consequences that are sometimes serious. With young patients, early or advanced, the danger to be feared is acidosis, and our therapeutic endeavors are directed to prevent its development or abolish it after development. When there is no acidosis I have never been compelled to resort to fast days as a means of controlling the most extreme glycosuria, although there is no doubt the end can be attained most rapidly by the complete withdrawal of food. The question is, then, is starvation always safe? It has been generally believed, and was emphatically stated by Neunyn, that an acidosis tendency once established is prone to recur. With diabetics as with normal persons, starvation induces acidosis, and even this, I think, can and should be avoided, since one can not tell where it may lead. Cases that I have seen in consultation have made me more definite in this impression. In two recent instances an alarming acidosis, initiated by fasting, necessitated heroic measures which availed to save the life of only one patient. These unfortunate issues we are not at present able to prevent unless the patient be in a hospital, and adequate warning of danger be watched for in the laboratory studies.

Turning now to cases in which acidosis dominates the picture and in which the disease is of long duration, the therapeutic problem is again different. The menace here is coma, and the fact that any of the patients can be relieved of their danger, even for a brief time

by fasting, is a *remarkable* contribution to our knowledge of diabetes. With cases that are in imminent danger of coma, in which each day may be the last, a measure that promises *any success at all* is of the greatest value; and here, I believe, is the special field for the fasting method. That fasting in itself may be a dangerous procedure, we recognize; as are also serious surgical measures. There are occasions when we have scant choice. That the fasting treatment is not devoid of hazard we must recognize, and it throws upon us the responsibility to use this method only when other and less drastic methods are inadequate to effect the desired result; and to recognize that fasting is, again, like many surgical measures, suited best for use in well-equipped hospitals, in which careful observation and frequent tests of blood, urine, and alveolar air are made as part of the routine. Only in this way can dangerous reactions be foreseen and requisite measures be instituted. The treatment is *fundamentally* a treatment for grave acidosis.

Finally, then, I can summarize my conclusions: Every case of diabetes demands the most careful study not only of the diabetic state, but also of all conditions which may influence the future health of the patient. Infections must be kept in mind as the constant danger. Early cases must be kept free of glycosuria in order to raise resistance and to avoid the development of acidosis. This can be done even in face of acidosis by the use of restricted low diets. With advanced cases glycosuria must be controlled in order to regain normal weight and vigor. When there is grave acidosis this also can now with many cases be successfully abolished. The chief difficulty in treating all diabetics is the necessity of constant vigilance over years.

THE EFFECT OF EXERCISE UPON THE CARBOHYDRATE TOLERANCE IN DIABETES.

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It has been known for many years that exercise increases the carbohydrate tolerance in the milder forms of diabetes, although in severe types of the disease it lowers the tolerance or may even precipitate coma. This therapeutic measure has been neglected, probably, because of the lack of a practical system of exercise the effects of which on patients could be checked up by an accurate test of the heart's functional capacity.

Our experience in treating patients with cardiac insufficiency by means of graduated exercise controlled by such a test, which we have described elsewhere,[1] suggested an experiment with these exercises on a few selected cases of diabetes.

The apparatus used consisted of dumb-bells weighing from 10 to 40 pounds each, and steel bars varying between 25 and 80 pounds in weight, with which different series of movements were carried out. The exercises were of a concentrated form, and were given an hour daily, three days in the week, generally in the late afternoon. Each series of movements lasted from thirty to one hundred and twenty seconds, and six to eight were given at each exercise period, so that the actual working time varied between four and sixteen minutes for the hour.

The first patient was a professional man, aged forty-two years, suffering from a mild form of diabetes. In November, 1909, an insurance company had discovered sugar in the urine. His tolerance at that time was 360 grams of white bread in twenty-four hours. His urine was kept practically sugar-free for the next four years. In June, 1913, his tolerance had decreased to 150 to 180 grams of white bread in the twenty-four hours. He was then put on one egg and vegetable day weekly. In October, 1913, his tolerance was still 150 grams, but by September, 1914, it had decreased to 120 grams.

On September 24, 1914, when the exercise course was started, the patient's physical examination was negative; he weighed 141 pounds and his lung capacity was 284 cubic inches.

The following table summarizes the results in this patient:

Date.	Quantity of carbohydrate (white bread) in twenty-four hours (grams).	Quantity of glucose in twenty-four hours' urine.	Approximate amount of work at each period in foot-pounds.
September 23, 1914	120	trace	14,900
October 19, 1914	150	none	
November 2, 1914	180	trace	21,700
November 9, 1914	180	none	
November 16, 1914	210	trace	
November 23, 1914	225	none	
November 30, 1914	240	3.1 grams	36,500
December 14, 1914	225	none	
February 1, 1915	240	none	40,000
March 17, 1915	270	trace	
April 24, 1915	270	trace	
May 12, 1915	270	trace	

During the period noted above the patient's daily allowance of carbohydrate was always kept well below his tolerance. An egg and vegetable day was given once weekly. His tolerance increased from less than 120 grams on September 23, 1914, to 240 grams on February 1, 1915. Although his exercises were continued until June 1, 1915, we never could get his capacity much beyond that

[1] Barringer and Teschner, Arch. Int. Med., 1915, xvi, p. 795.

figure. He gained six and one-fourth pounds in weight and his lung capacity increased from 284 cubic inches to 300 cubic inches. His general health and ability to do his work without fatigue improved markedly.

These results are truly astonishing when we consider that the actual working time of our patient during his course of fifty exercise periods amounted to between four and sixteen hours.

July 1, 1915, he stopped the exercises and in their stead lead an active outdoor life in the country for ten weeks. His exercise there was carried out quite systematically, and consisted chiefly in chopping down trees, chopping wood, and using a pick on a clam-shell road. He continued his weekly egg and vegetable day and kept his daily intake of carbohydrate well within his tolerance. To our surprise the tolerance decreased steadily, as is seen by the following table:

Date.	Quantity of carbohydrate (white bread) in twenty-four hours. (grams).	Quantity of glucose in twenty-four hour-specimen.
August 3, 1915	225	trace
August 13, 1915	195	trace
August 31, 1915	165	trace
September 20, 1915	120	none
October 5, 1915	150	none
November 21, 1915	180	trace
December 5, 1915	180	trace
December 19, 1915	195	trace
January 2, 1916	195	trace

On September 20 the patient returned to the city and resumed his dumb-bell and bar exercises. Through a misunderstanding he did them each day before breakfast, but on December 5 this was remedied. Also for three weeks they were omitted on account of an attack of lumbago. He now seems (December 19) to be approaching his former tolerance of 240 grams.

The second case selected was one of moderate severity. The patient was a professional man, aged thirty years, in whom a glycosuria had been discovered in 1912. Since then, in spite of following quite conscientiously a treatment initiated by Dr. von Noorden, his urine never has been sugar-free.

The following table summarizes our results:

Date.	Diet.	Glucose in twenty-four hour-specimen.	Exercise.
February 28, 1915	6 days carbohydrate-free	7.9 gms. (acetone +)	
March 16, 1915	60 gms. white bread	14.4 gms. (acetone 0)	
April 1, 1915	30 gms. white bread 150 gms. oatmeal	6.4 gms.	Three hours weekly, began March 20.
April 17, 1915	30 gms. white bread 150 gms. oatmeal	4.6 gms.	
May 1, 1915	30 gms. white bread 150 gms. oatmeal	10.2 gms.	
May 7, 1915	Egg and vegetable day	6.3 gms.	

This patient's weight increased from 135¼ pounds to 140½ pounds, but the glycosuria was not at all influenced. His general health and ability to work were markedly improved.

The third patient was a business man, aged sixty-four years, who had had a mild diabetes for about five years, his tolerance being 60 grams of white bread in twenty-four hours. This was increased to 90 grams of bread after an extended course of exercises.

SOME ASPECTS OF THE CLINICAL STUDY OF THE RESPIRATION: THE SIGNIFICANCE OF ALVEOLAR AIR ANALYSES.[1]

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One of the most striking developments in clinical medicine during the last decade has been the gradual substitution of the physiological for the anatomical point of view. Up to within a comparatively few years the chief basis of medicine was pathological morphology, and the chief aim of diagnosis was to determine the anatomical changes in the diseased organs. Recent advances in physiology and in biological chemistry, however, have exerted a profound influence on the attitude of the clinician, and have impressed on him the importance of approaching his subject from a much broader aspect. The problem of diagnosis is now not so much to discover what a given organ may look like, but what it is doing or what it is able to do. Pathological physiology is becoming more and more an object of investigation, and such terms as "functional tests" and "functional diagnosis" are already current in medical phraseology.

The application of the methods of physiology has already produced an abundant harvest of results in several fields. The study of polygraphic tracings and of electrocardiograms, both in man and in experimentally produced conditions in animals, has quite altered our conceptions of heart disease. New clinical conditions have been differentiated, and processes long recognized have been explained. In renal diseases the "functional studies" have thrown new light on the various types of nephritis, their course, prognosis, and treatment. Some progress has been made in the investigation of hepatic function in disease, but as yet, unfortunately, little of great clinical significance has been brought out. On the subject

[1] Read before the Springfield Academy of Medicine, March 9, 1915.

of respiration a large amount of important work has already been done. The greater part of this has had to do directly with the study of metabolism, of oxygen intake, and carbon dioxide output and their relation to heat production under various conditions. Until comparatively recently very little attention has been paid to the abnormalities of respiration itself, but the development of a more comprehensive knowledge of the physiology of respiration and the adaptation of new physiological and chemical methods have opened up fresh paths to clinical investigation.

From the point of view of clinical medicine some of the most significant of the recent investigations on the physiology of the respiration have been those dealing with the determination of the normal stimulus to respiration. Among the older physiologists one school held that the respiratory centre was stimulated by a lack of oxygen, while their opponents claimed that it responded to an excess of carbon dioxide in the blood. The work of Haldane and Priestley,[2] in 1905, settled the problem for the time being and seemed to prove conclusively that carbon dioxide is the effective stimulus to respiration. Their experiments showed that the respiratory centre is extremely sensitive to changes in the tension of the carbon dioxide in the blood. A rise of 0.2 per cent. in the carbon dioxide of the alveolar air was sufficient to double the pulmonary ventilation, while a fall below the normal resulted in the production of apnea. Subsequent work, especially that of Winterstein[3] and of Hasselbalch[4] showed that the action of carbon dioxide as a stimulus to respiration is not specific, but that it depends on the fact that carbon dioxide is an acid. Any other acid can replace carbon dioxide wholly or in part as the stimulus. Indeed, it has been definitely demonstrated that the respiration depends on the reaction of the blood, or, as it is technically called, on the hydrogen-ion concentration of the blood. Under normal conditions the reaction of the blood is very slightly on the alkaline side of the neutral point. Any tendency toward an increase in the acidity, whether it be caused by an accumulation of carbon dioxide, or of any other acid, acts as a stimulus to the respiratory centre and increases the ventilation of the lungs. Even the increase of respiration, which is caused by an insufficient supply of oxygen reaching the tissues, may be explained by this same mechanism, for one of the results of imperfect oxidation is the incomplete combustion of acid products of metabolism, and these intermediary metabolites, insofar as they are acids, may form a part of the respiratory stimulus.

Since, then, the chemical control of the respiration depends on the reaction of the blood, it will be readily seen that in order to understand the pathological changes in respiration one must bear

[2] Jour. of Physiol., 1905, xxxii, 225.
[3] Arch. f. die ges. Physiol., 1911, cxxxviii, 167.
[4] Biochem. Ztschr., 1912, xlvi, 403.

in mind the conditions which regulate the reaction of blood. Henderson[5] has said that the normal reaction of blood is, like the normal body temperature, one of the important physiological constants. All modern work bears this out. The chemical processes within the body, and especially all enzyme reactions, proceed most advantageously at an optimum hydrogen-ion concentration, and for many the range of reaction through which they can function is a narrow one. Life itself depends on the maintenance of the reaction of blood and tissues within very small normal limits. Undoubtedly the fundamental problem is that of the maintenance of the normal reaction within the tissue cells, for in all probability most of the important chemical processes by which metabolism is carried on are intracellular, or at least are the result of the actions of substances formed within the cells, whose very formation and elimination into the blood depends on the balance of acid and alkali within the cell. At the present time there are no very refined methods of studying tissue reaction, though, as will be shown later, the so-called "alkali-tolerance" test seems to give a more or less rough index of any continued overproduction of acid in the body and of consequent exhaustion of the reserve alkali of the tissues. Until methods have been evolved which will lead us into the obscure field of cellular and of tissue metabolism we must be content with studies of the blood. The composition of the blood certainly depends in large part on the activities of the fixed cells of the tissues, and the newer investigations of the chemistry of the blood and of the intermediary products of metabolism which it contains are leading to a much more intimate knowledge of the chemical processes of the body than could ever be obtained by examinations of the excretions alone. In the maintenance of the normality of the tissue reaction the blood plays an important part. It carries bases to the tissues to replace those used in neutralizing acids, and it forms the medium by which the acid products of cellular activity are removed from the cell. Fortunately, however, in spite of the fact that carbon dioxide and other acid products of metabolism are continually passing into the blood, the organism is peculiarly well provided with means to preserve its normality. That the reaction of the blood is not affected by this addition of acids depends (1) on its chemical composition, and (2) on the means at its disposal for the rapid excretion of acids.

The chemical composition of blood is such that it is ideally adapted for the preservation of a constant reaction. It contains large amounts of weak acids and their salts—carbon dioxide and sodium bicarbonate, monosodium phosphate and disodium phosphate—and a high percentage of proteids which have both basic and acid characteristics. To solutions which are made up of such

[5] Science, 1913, N. S., xxxvii, 389.

combinations it is possible to add considerable quantities of acid without producing any marked change in the hydrogen-ion concentration. If, for instance, acid be poured into a solution consisting of monosodium and disodium phosphates, the balance between the two will be disturbed—there will be more of the monosodium phosphate and less of the disodium phosphate—but within rather wide limits there will be only a minimal alteration in the true reaction of the solution. Indeed, Henderson has shown that the balance of weak acids and salts in blood is such as to allow of the addition of the maximum amount of acid with the minimum alteration in reaction.

The constancy of the reaction of blood is furthermore upheld by the means which the body has at its command for the excretion of acid. Non-volatile acids are excreted by the kidneys. Henderson[6] has drawn particular attention to the remarkable efficiency of the kidneys for their task. By some specific mechanism they are able to separate acid from bases, secrete an acid urine from an alkaline blood, and retain base in the body for the further neutralization of more acid. Volatile acids, and chiefly, of course, carbon dioxide, are excreted in the lungs. In the pulmonary capillaries carbon dioxide passes out of the blood into the air of the alveoli until the carbon dioxide tension in the blood equals that in the alveolar air. Thus the tension of the carbon dioxide in the alveolar air corresponds to that of the blood, and, as will be seen, it is an index of acidosis. In their function of excreting acid the kidneys may perhaps be regarded as the fundamental regulators of the reaction of the blood, but as the lungs are much more sensitive they can maintain extremely delicately the constancy of reaction by their control over the volatile acids.

Any rise in the acidity of the blood stimulates the lungs to increased ventilation. With moderate exercise there is an increased production of carbon dioxide in the tissues. If this is sufficient to affect the arterial blood to the respiratory centre, the pulmonary ventilation rises and more carbon dioxide is excreted. The same happens when air is rebreathed from a closed space. The carbon dioxide in the inspired air, and consequently in the alveoli, rises. This causes a rise of carbon dioxide tension in the blood and and an increased ventilation of the lungs. During severe exercises, lactic acid is produced more quickly than it is excreted by the kidneys, and Ryffel[7] has shown that it is increased in the blood.

Under such circumstances the lactic acid acts as a stimulus to respiration by increasing the acidity of the blood. The lungs respond, but in order to keep the hydrogen-ion concentration of the blood at its normal level there must be a reduction of the

[6] Jour. Biol. Chem., 1911, ix, 403.
[7] Jour. Physiol., Proc. Physiol. Soc., 1910, xxxix.

carbon dioxide below its normal. Thus associated with the rise in non-volatile acids there is a compensatory decrease in the carbon dioxide tension of the blood, and since the two correspond, in the carbon dioxide tension of the alveolar air. These conditions are indicated diagrammatically in Figs. 1 and 2.

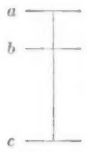

FIG. 1

FIG. 2

In Fig. 1 the line a–c represents the acidity of normal blood; b–c is acidity due to non-volatile acids, and a–b is the acidity due to carbon dioxide.

Fig. 2 represents the conditions in acidosis due to a rise in the non-volatile acids, such as lactic acid in hard exercise or β-oxybutyric acid in diabetes, b'–c', which is longer than b–c in Fig. 1, represents the increased acidity due to non-volatile acids. If the carbon dioxide remained unchanged, the acidity of the blood would be represented by the line d'–c', an increase in the acidity of the blood which the organism could not withstand. In order to keep the acidity of the blood at its normal value, a'–c', the rise in non-volatile acids is compensated for by a fall in carbon dioxide, so that the amount of carbon dioxide or, more accurately, the carbon dioxide tension, is reduced to a'–b'. Thus in conditions of acidosis the tension of the carbon dioxide in the blood or, what is the same thing, the tension of carbon dioxide in the alveolar air, gives an accurate index of the amount of the increase of non-volatile acid.

The demonstration that one of the chief functions of the respiration is to preserve the normal reaction of the blood, and that any increase in the acidity of blood acts as a stimulus to respiration, is of great importance in the consideration of pathological changes in the respiration. In the study of acidosis—of the increase of normal acids or the presence of abnormal acids in the blood—we possess a means of acquiring information concerning the stimulus to respiration and its variations in abnormal conditions. There are several general methods of approach by which one may find out about the formation of acids in the body. The examination of the urine with reference to its acidity, and to the presence of abnormal acids, while of a certain value, only tells about the acid which is leaving the body and does not necessarily give an accurate picture of conditions within the body. Of much more significance are studies of the blood itself. As has already been stated, the true reaction of the blood varies extremely slightly during life. Only in terminal

conditions has any marked deviation from the normal been found. Thus in most clinical conditions one does not expect that an increase in the formation of acids in the body will cause any actual change in the reaction of the blood, but merely a shift in the usual balance between volatile and non-volatile acids. In the pathological conditions associated with acidosis there is usually an increase in non-volatile acids and a consequent fall in carbon dioxide. The evidence of the presence of such a state may be obtained from the study of the blood or of the alveolar air, for the carbon dioxide tension of the alveolar air is the same as that of the blood.

The determination of the hydrogen-ion concentration of the blood is a complicated procedure. On account of its color, the high percentage of protein, and the influence of the carbon dioxide the simple colorimetric methods which may be used in urine are not practicable. The direct determination can only be carried out by means of electrochemical methods, and the difficulties of the technic are considerably enhanced by the importance of measuring the blood at a known carbon dioxide tension.[8] Barcroft[9] has devised a method by which the acidity of the blood is determined from the affinity which the hemoglobin shows for combining with oxygen under standard conditions. Both of these methods involve a highly specialized technic, but fortunately a very valuable index of the conditions in the blood may be obtained quite simply by means of an analysis of the alveolar air.

Under normal conditions, at rest, the carbon dioxide tension of the alveolar air is fairly constant. It shows only slight variations in different individuals, and in the same individuals at different times of day. The normal diurnal variations depend chiefly on diet. Thus on a pure carbohydrate diet the carbon dioxide extension is at a high level, while on a diet consisting largely of proteid or during starvation the tension tends to be lower. The normal variations, however, involve only a few millimeters and do not detract from the value of the determination in pathological conditions.

Samples of alveolar air may be obtained by several methods:[10] The first to be introduced was that of Haldane. In this method the subject gives a long, deep expiration into a piece of rubber tubing about four feet long. At the end of the expiration the entrance of the tubing is closed by the subject's tongue or by some form of valve, so that the expiration is held in the tube. By means of a small side tap near the mouth-piece, 25 to 50 c.c. of the air which constitutes the last portion of the expiration are withdrawn into a mercury filled gas pipette and subsequently analyzed. The last

[8] Arch. Int. Med., 1914, xiv, 236.
[9] The Respiratory Function of the Blood, 1914, Camb. Univ. Press.
[10] Arch. Int. Med., 1914, xiii, 497.

part of the expiration, particularly if the expiration is at least 600 c.c. deep, comes from the alveoli of the lungs, and if the expiration is sufficiently rapid its composition remains practically unchanged in its passage outward. In the hands of trained persons this method gives reliable results, and the figures obtained for carbon dioxide tension probably agree very closely with that of the arterial blood. Even with untrained subjects it is frequently possible to get satisfactory samples, but as it is necessary to have a very deep and rather rapid expiration there are many times when the method is unreliable. This is especially apt to be the case with persons of low intelligence or with patients who are sick and unable or unwilling to give a complete expiration. In such instances the method of Plesch as modified by Higgins[11] gives excellent results. A large series of observations made during the last two years at the Peter Bent Brigham Hospital with this method has demonstrated its simplicity and reliability in a considerable variety of clinical conditions. The method is based on the principle that if the subject breathes into and out from a closed space of suitable size for a definite period of time the diffusion of gases will be such that the composition of the air in the closed space will be similar to that in the lungs. In practice the nose is closed with a clip and the patient breathes through a mouth-piece, which is connected with a three-way valve leading to the outside air or into a rubber bag. The subject begins by breathing the outside air. At the end of an expiration the valve is turned so that the subject is connected with the rubber bag which contains about 1 liter of air. He takes four or five rather deep and slow respirations from the bag in twenty or twenty-five seconds. At the end of the last expiration the valve is again turned and the subject connected with the outside air. The bag, which is closed off by the same maneuver, contains air which is of the same composition as the air in the alveoli. Samples are then taken from the bag for analysis. The figures obtained for carbon dioxide tension by this method are somewhat higher than those obtained by the Haldane method, and they probably represent more nearly the tension of the carbon dioxide in the venous blood than in the arterial blood. In physiological studies the difference would be important, but in most clinical work the Plesch method gives results that fulfil all the necessary requirements. There are two chief sources of error in the method: The figures for carbon dioxide tension are too low if the respirations are very rapid and shallow, so that proper diffusion of gases does not take place. The results are too high if the subject is permitted to breathe from the bag for a period which exceeds in length one complete cycle of the circulation or approximately forty seconds. In general, however, constant and reliable results are obtained with little

[11] Pub. No. 203, Carnegie Institution of Washington, 1915, p. 168.

experience. Three observations are usually made, and the analysis of the samples should agree within 2 mm. carbon dioxide tension. Occasionally one of the three varies so far from the mean that it has to be discarded. The analysis of air for carbon dioxide is extremely simple. By means of the Haldane gas analysis apparatus it can readily be completed in about four minutes. The figures for the normal tension of carbon dioxide in the alveolar air vary from about 38 to 41 mm. by the Haldane method and from 40 to 45 mm. by the Plesch method.

Results of the Study of Pathological Conditions. Diabetes. One of the first diseases in which it was recognized that acidosis played an important part and the disease in which the effect of acidosis on the respiration is most definitely manifested is *diabetes*. Probably on account of the incomplete or imperfect combustion of fats in severe cases of diabetes there may accumulate in the organism large amounts of β-oxybutyric acid, aceto-acetic acid, and acetone—substances which under normal conditions would be completely burned to water and carbon dioxide. This abnormal production of acids may go on for a long time without giving rise to any clinical symptoms, but when it reaches an extreme grade it becomes the most prominent feature in the case and eventually brings on the well-known clinical picture of "air hunger" and coma. During the early stage, while the production of acids is not excessive, the bases in the tissues and in the blood are sufficient to neutralize them, and their excretion is accomplished by the kidneys. At this period the ordinary mechanisms of the body are amply able to cope with the acidosis, so that there is no tendency for the reaction of the blood to be disturbed. If the condition continues, however, and the amount of acid increases, the reserve supply of base in the tissues will become exhausted in the attempt to neutralize the acid. The blood itself will be able to take up a considerable amount of acid without any effect on its true reaction, but beyond a certain point the addition of more acid will tend to cause a shift in the reaction of the blood. This increase in acidity will act as a stimulus to respiration and the normal reaction of the blood will be maintained by an increased pulmonary ventilation and a lowering of the carbon dioxide tension of the blood. The balance in the blood will be disturbed and there will be an increase in non-volatile acids with a corresponding drop in the tension of the carbon dioxide in the blood and in the alveolar air. This is the beginning of serious acidosis. The reserve supply of base in the tissues has been used up, the regulatory mechanism in the blood has begun to break down, and the organism is calling on its last reserves. If the condition progresses there will be a steady fall in the carbon dioxide tension of the blood until the symptoms of poisoning assert themselves. Finally the production of acids becomes so great that even kidneys and lungs together are unable

to excrete enough acid to keep the reaction of the blood within its normal bounds. The increased acidity of the blood stimulates the respiratory centre to greater efforts, and there results the enormous ventilation marked by the deep, rapid breathing which is so well termed "air hunger." Unless the formation of acids is reduced or their neutralization is brought about by some means, death from acidosis will ensue.

There are several methods by which it is customary to follow the course of acidosis in diabetes. Since these are usually tests applied to the urine they give evidence only of the amount of acid which is being excreted from the body. They give extremely unreliable information as to the amount of acid which is being formed in the body and as to the amount which is accumulating in the body. These latter are, after all, the factors of importance. What one wants to know is not how much acid the organism is getting rid of, but how much it is retaining, for it is the retained acid that is the source of danger. The commonest tests applied in diabetic acidosis are the qualitative tests for acetone and aceto-acetic acid. The attempt is usually made to get a general idea of the amount of each acid excreted from the degree of the reaction. The value of these tests is limited both by the fact that they give no conception as to the excretion of β-oxybutyric acid and because the information they do give may throw so little or such false light on the actual conditions within the body that an implicit reliance on them becomes extremely dangerous. In severe acidosis, and even in diabetic coma, the ferric chloride reaction is sometimes very weak. After the administration of alkali the reaction frequently becomes much more intense. On the one hand the patient may have been in grave danger from acidosis at the time when the urine showed evidence of a very small aceto-acetic acid excretion, while, on the other hand, the increase of the excretion of aceto-acetic acid may have been accompanied by a return to conditions within the body which are comparatively normal. Not infrequently one hears of cases of diabetes that went suddenly into coma without any previous warning. These are probably instances in which there has been an accumulation of acid in the body without any very marked excretion in the urine, so that even careful urine examinations have failed to call attention to the impending danger. It seems probable that the ammonia excretion is the best index which can be obtained from the urine, but even this will fail to give a correct quantitative picture in certain instances. As Poulton[12] has pointed out the ammonia in the urine depends (1) on its production in the body, and (2) on its excretion by the kidneys, and if either of these functions is disturbed the values obtained will fail to give a true estimate of the acidosis. It is, moreover, the total

[12] Proc. Roy. Soc. Med., 1914, vii (Med. Sec.), 171.

amount of ammonia excreted in twenty-four hours that is of importance, and in many cases it is impossible to obtain complete collections of urine. Even at best the method does not allow one to obtain the immediate information that is so often desirable. The determination of B-oxybutyric acid in the blood would be of great value, but the methods now available are difficult and require a considerable amount of time. On the whole the determination of the carbon dioxide content of the alveolar air bids fair to prove one of the most useful aids in judging of the severity and course of acidosis. It is comparatively simply done, and it gives accurate information of the conditions which prevail in the blood at any given time. The presence of a positive ferric chloride reaction in the urine shows that abnormal acids are being formed, but if at the same time the alveolar air remains normal it is probable there is no immediate danger to be feared. When the alveolar carbon dioxide falls below normal the danger zone is being approached. Values between 35 and 30 mm. may be taken as indicating the development of a considerable acidosis, and one that demands treatment, but they need not give rise to the fear of any serious complication. Carbon dioxide tensions between 30 and 20 mm. are of much more significance, and are to be regarded as evidence that the patient is nearing the border-line and must be watched with great care. A constantly falling carbon dioxide tension is a serious warning, and is of great prognostic value. If the carbon dioxide tension is down to 20 mm. or lower the patient has reached a state in which coma may suddenly appear. Indeed, Poulton[13] who has given this matter considerable attention, states that "values of below 2.5 per cent. (about 18 mm.) indicate the early onset of coma, possibly within forty-eight hours unless drastic measures are taken." Analyses of the alveolar air in a case which was recently admitted to the Peter Bent Brigham Hospital in diabetic coma showed that the carbon dioxide tension varied between 6 and 10 mm. Very similar figures are given by Poulton for his cases in coma.

Besides being an aid to prognosis the alveolar air determinations may be of distinct value as a guide to therapy. When alkali is being administered the urine gives little evidence as to the results that are being accomplished until its reaction has been changed. As has already been stated, the ferric chloride reaction often becomes more intense. The alveolar air, however, gives an accurate indication of the effect of treatment. As the acidosis is overcome the carbon dioxide tension rises until it reaches normal. At this point the patient is out of immediate danger, but frequent examinations will be necessary to keep one informed as to when vigorous treatment may have to be instituted again. This effect of the alkali is

[13] Proc. Roy. Soc. Med., 1914, vii (Med. Sec.), 171.

usually rapid and complete in cases of mild or moderate acidosis, but if the acidosis has developed to an extreme grade, a point is apparently reached beyond which the administration of alkali produces little or no permanent change in the clinical picture or in the composition of the alveolar air. Thus in the patient with diabetic coma mentioned above, in spite of the administration of considerable amounts of sodium bicarbonate, both by mouth and intravenously, no permanent beneficial effect was produced. On admission, shortly after he had gone into coma, the alveolar carbon dioxide was 6.71 mm. After vigorous treatment it rose to 10.7 mm. on the next day, and synchronous with this his mental condition improved so that he was recognizing his friends. On the following day the carbon dioxide tension was 12.9 mm. and there was further subjective improvement. During the night, however, his condition suddenly changed and he went rapidly into a diabetic coma in which treatment was without avail and which was fatal within twenty-four hours. It is, of course, possible that much larger amounts of alkali should have been given, and perhaps such treatment would be safe if it were guided by alveolar-air determinations.

Chronic Nephritis. Among the many theories which have been brought forward to explain the clinical picture of uremia is that which acounts for it on the basis of an acidosis. As early as 1888 von Jaksch[14] suggested that this was the underlying factor. During the last few years this theory has again been brought into prominence by the work of Straub and Schlayer,[15] on the alveolar air in advanced cases of nephritis, and by the studies of Sellards[16] and Palmer,[17] both of whom showed that a mild grade of acidosis may be present comparatively early in the course of the disease. Evidence of the existence of an acidosis in moderate cases of chronic nephritis is based in large part on the so-called "alkali-tolerance" test of Sellards. If a normal individual be given sodium bicarbonate the urine will become alkaline after the ingestion of 5 grams or, at the most, of 10 grams. If an acidosis is present a much larger amount of alkali will be needed to produce this change in reaction. The probable explanation of this is that during the development of the acidosis the reserve supply of base in the tissues is being drawn upon to neutralize the acids which are produced. When more base is supplied to the body by the administration of alkali this is first used to restock the depleted stores in the tissues before it is allowed to accumulate in the blood and bring about a change in the reaction of the urine. If this theory of the mechanism by which the body disposes of alkali, when it is administered to it during acidosis is correct—and there is every

[14] Ztschr. f. klin. Med., 1888, xiii, 350.
[15] München. med. Wchnschr., 1912, lix, 569.
[16] Johns Hopkins Hosp. Bull., 1912, xxiii, 289; ibid., 1914, xxv, 141.
[17] Med. Communication, Massachusetts Med. Soc., 1913, xxiv, 133.

reason to suppose that it is—then it will be seen that the "alkali-tolerance" test may serve as an important index of what may be termed "tissue acidosis." Since the acid products of metabolism are largely formed within the cells, it is evident that "tissue acidosis" may occur before there will be any marked change in the blood. Probably only after large amounts of acid have been produced in the cells, and the supply of bases in the cells has been to a considerable extent used up, will unneutralized acid pass into the blood, and only after the blood itself has neutralized much of this will the composition of the blood be changed in the sense of an increased acid reaction. Thus quite a degree of acidosis may exist in the body without affecting the blood so as to cause a fall in the carbon dioxide tension of the alveolar air.

The "alkali-tolerance" test throws much light on the time of the development of acidosis in renal disease and on its underlying causes.[18] In early cases of nephritis, such as those in which the phthalein test shows a normal excretion, even when they are accompanied by a pronounced hypertension, it is unusual to find any evidence of acidosis. The urine is readily made alkaline by the administration of 5 to 10 grams of sodium bicarbonate. As cases become more severe and the phthalein excretion begins to drop below the normal level the "alkali-tolerance" test is likely to become increased, so that 15 to 20 grams of sodium bicarbonate are required to change the reaction of the urine. As the nephritis progresses and phthalein excretion continues to decrease the "alkali tolerance" rises until, in very advanced cases, it may be extremely difficult to administer sufficient base to make the urine alkaline. The development of the acidosis thus bears a definite relationship to the functional capacity of the kidney as indicated by the phthalein test. The fall in phthalein output runs fairly parallel with the rise in non-protein nitrogen content of the blood, and it is natural to refer both of these, and also the acidosis which accompanies them, to the decrease in the excretory power of the kidney. The acidosis of chronic nephritis is thus due to retention. While in diabetes the acidosis is the result of increased formation of acids, in nephritis it apparently depends on the inability of the organism to get rid of even a normal amount of acid. Whether there is also in nephritis a production of acids which exceeds the normal is as yet an uncertain question. The experimental work of Mosenthal,[19] which seems to show that a toxic destruction of protein is one of the accompaniments of nephritis, would favor such a view, for it is well known that proteids give rise to large amounts of acid-combustion products.

The urine in nephritis gives little information as to the acidosis within the body—even less than does the urine in diabetes. The

[18] Results to be published in detail in a separate communication.
[19] Arch. Int. Med., 1914, xiv, 844.

hydrogen-ion concentration may be high, but it rarely exceeds the normal limits, and high values are by no means constant. The ammonia in the urine may not be increased, and is a comparatively unimportant index, as much of it may be retained with the other nitrogenous decomposition products. The ferric chloride reaction if positive is usually weak. The acidosis of nephritis is not due to the acetone bodies, but as to what acids are retained in the body little is known.

While urine analysis is of limited significance in determining the grade and character of the acidosis in nephritis, much can be gained from observations on the alvolar air. A study of about 50 cases in all stages of the disease permits of several general deductions on the manner and extent of its development. In the early stages of the disease there is no accumulation of non-volatile acids in the blood such as to cause a deviation of the tension of the alveolar carbon dioxide from the normal. Even after the phthalein excretion falls below normal, and after the "alkali-tolerance" test shows evidence of a considerable degree of "tisssue acidosis," there is rarely any change in the alveolar air. Insofar as the acids are not excreted by the kidney they are apparently taken up by the blood, but the amount is not sufficient to cause any change in the reaction of the blood. At the time when the phthalein excretion is very low, and more often when there is no phthalein excretion, one frequently begins to find a drop in the alveolar carbon dioxide tension. This, however, is not a constant finding, as one patient with no excretion of phthalein and with non-protein blood nitrogen up to 90 mg. per 100 c.c. of blood had an alveolar carbon dioxide tension of 40.3 mm. ten days before she died. The majority of patients have a slight or moderate decrease of carbon dioxide, with values ranging from 37 to 25 mm. Such figures may be found during the development of uremia, but when the condition advances to coma the acidosis is frequently of higher grade. Nevertheless, in advanced uremia the alveolar carbon dioxide may not be below 30 mm. One patient had a carbon dioxide tension of 33.8 mm. and another of 24.4 mm. on the day before death. In certain cases, however, the onset of uremia is accompanied by the occurrence of a sudden and severe acidosis. In two instances the carbon dioxide fell to 4.59 and 19.1 mm. respectively. Both of these patients presented the clinical picture which is seen in diabetic coma, and their respiration was increased so that it amounts to a true "air hunger." The former died on the day after the alveolar air was examined. The latter was unusually interesting in the response shown to alkali therapy. The patient was a woman, aged forty-five years, with a history of nephritis going back for several years. Her blood-pressure was about 200 mm., and the non-protein nitrogen in her blood had risen to 90 mg. per 100 c.c. of blood. For over a month the phthalein test had shown practically no

elimination of the dye in the urine. In spite of the very advanced nephritis her general condition remained fair, and except for headache there was no evidence of uremia until January 11. On this day she first began to complain of being short of breath. The alveolar carbon dioxide was 19.1 mm. tension. Turning over in bed caused marked dyspnea. Two days later, January 13, the patient was unconscious and her respiration was slow, but so deep as to be quite typical of "air hunger." The alveolar air was not taken at this time, but 300 c.c. of 4 per cent. sodium bicarbonate solution were given intravenously. On the following morning the carbon dioxide tension was 23.4 mm. This indicated a marked acidosis, and as the "air hunger" persisted, a further intravenous injection of 700 c.c. was given later in the day. When the patient was seen on the next morning the clinical picture had entirely changed. She was quite conscious, recognizing every one, but was greatly nauseated and looked very sick. The "air hunger" had disappeared, and the respiration was shallow, slow, and irregular, with rather prolonged periods of apnea. The alveolar carbon dioxide tension had risen to the normal value of 41.5 mm. On the next morning it had fallen to 36.9 mm. Respiration was perhaps slightly deeper, but did not suggest "air hunger." There were occasional deep, sighing breaths. Her sensorium was clouded, but she was conscious and responded fairly well to questions. In an attempt to ward off the further development of acidosis, 375 c.c. of 5 per cent. sodium bicarbonate were given intravenously, but in spite of this the alveolar carbon dioxide had next day dropped to 25.1 mm., her respiration was deeper and more rapid, and she was becoming unconscious again. On January 17 she was comatose and had begun to have convulsions. Respiration was deep, irregular, and stertorous. It was extremely difficult to get satisfactory samples of alveolar air. Those obtained showed a carbon dioxide tension of about 30 mm. Another intravenous alkali injection was without effect, and the patient died on January 18. This case is reported in considerable detail because it shows unusually well the development of a marked acidosis during uremia, which was clinically similar to the typical acidosis of diabetes. The existence of the acidosis was confirmed by the alveolar-air examinations, with its response to alkali treatment was, though temporary, most striking.

The demonstration of the occurrence of acidosis in chronic nephritis is a comparatively simple matter. It is much more difficult to form a correct opinion as to the part which the acidosis plays in the symptomatology of nephritis and of uremia. To do so on the basis of the knowledge now at our command would probably be impossible. So complex are the changes in the blood and tissues which may result from the inability of the kidneys to excrete the waste products of metabolism, and so many are the substances which may accumulate in the body, that it is not

easy to determine what effects any one of them may produce. However, in a condition like uremia it is most important to separate out the constituent causative elements, for only by so doing will its pathology eventually become clear. It is, of course, possible that the accumulation of acid and the consumption of the supply of base in the tissues, even as it occurs during the early period of retention, may have some abnormal effect on the fixed cells. If there is any such it is obscure, and at present there is no evidence as to how it acts. In the later stages, especially with the change in the blood and the fall in the alveolar carbon dioxide, the acidosis, as will be shown later, seems to bear a relation to the occurrence of dyspnea. The association of acidosis and uremia is of special interest. The extent to which acidosis appears in and causes the symptom-complex of uremia is a variable one, but it seems to be an element in most if not all cases. In one group of patients uremia may exist for a considerable period and the acidosis be of a grade that produces a high "alkali tolerance," but only a slight depression of the alveolar carbon dioxide. With the onset of coma the alveolar carbon dioxide will perhaps drop somewhat, but there is no development of "air hunger," nor does the carbon dioxide tension reach the values seen in diabetic coma. Other patients present a picture in which the acidosis is in the foreground. With the onset of severe uremia at or just before the time when coma sets in the clinical signs of acidosis present themselves, the respiration is similar to that in diabetic coma, and the alveolar carbon dioxide will be found to have dropped to the very low values which obtain in that condition.

The single experience cited above shows that this type of case will, at least sometimes, respond to alkali treatment. The response will probably only be temporary, for uremia is not acidosis alone, and even if the acidosis is successfully combated, there are other factors which must eventually bring about death.

Cardiac Dyspnea. Some of the newer methods for studying the physiology of the respiration have also been applied in an attempt to explain the etiology of cardiac dyspnea. While there are as yet many points that are uncertain, progress has been made, and the facts so far determined are of importance to the clinician. Lewis, Barcroft, and their collaborators were the first to point out that in considering this problem one must recognize two groups of dyspneic patients. One of these consists of the pure cardiac cases. "These are usually young subjects with fresh or heightened color, and although cyanosis—slight, moderate, or deep—is present, dyspnea, as indicated by the rate of respiration, is not great. The respirations range from twenty-five to thirty-five per minute; orthopnea is present and the field of respiratory response is strictly limited."[20] The other group consists of elderly subjects with con-

[20] Quart. Jour. Med., 1915, viii, 97.

tinuous dyspnea, often intensified for short periods, especially at night, without marked cyanosis, with Cheyne-Stokes breathing, an increased pulse rate, and a subnormal temperature. The clinical picture is essentially what is generally known as cardiorenal disease. Further studies have confirmed the desirability of differentiating these two groups, partly on account of their clinical symptomatology and partly because the cause of the dyspnea is not quite the same in both classes.

The group of pure cardiac cases with dyspnea consists chiefly of patients with valvular disease and acute decompensation. They are often extremely breathless when first brought to the hospital, but it is quite striking that severe dyspnea does not generally persist for long. After one or two days the respiration usually becomes much quieter, although orthopnea may continue for some time. While dyspnea is produced by very slight exertion, they are comparatively comfortable as long as they are at rest in bed. In an attempt to obtain some information as to the cause of the dyspnea in this group of cases the alveolar carbon dioxide has been studied and the following facts obtained. At a time when the patients show no dyspnea while they are at rest, even though very slight exertion causes breathlessness, the alveolar air is perfectly normal. Very frequently during the period of dyspnea the alveolar carbon dioxide shows no evidence of acidosis. Indeed, the absence of acidosis is, according to Lewis and his associates, one of the characteristics of this type of case. Since they have failed to find any evidence of acidosis by using Barcroft's method for the blood, and since the dyspnea and the cyanosis seem to them to run nearly parallel, they believe that the dyspnea depends on poor oxygenation of the tissues. The studies at the Peter Bent Brigham Hospital, however, have demonstrated that in many cases at the time when the dyspnea is most severe the alveolar air analyses show a depression of carbon dioxide tension such as indicates a moderate grade of acidosis. Thus, two patients who entered the hospital with severe dyspnea and a high degree of cyanosis showed carbon dioxide tensions of 30.9 and 34.7 mm. respectively. A few days later, when they had regained compensation, the alveolar air had returned to normal. It is noteworthy that the phthalein tests, the nonprotein nitrogen in the blood, and the blood-pressure were normal in these patients, so there is nothing to make one believe that there was any renal element in the case. These observations on the acidosis of cardiac dyspnea confirm the results of Beddard and Pembrey[21] and of Porges, Leimdörfer, and Markovici.[22]

Thus in the pure cardiac cases dyspnea may be present when the alveolar carbon dioxide is normal or when it is somewhat

[21] British Med. Jour., 1908, ii. 580.
[22] Ztschr. f. klin. Med., 1913, lxxvii, 446.

depressed. In other words, there may or may not be acidosis, and if there is any acidosis, it is usually present only during the very acute stage, after which it quickly disappears. In either case the dyspnea is probably correctly explained by Lewis as the result of insufficient oxygenation of the tissues. With the failing heart and slowing of the circulation, carbon dioxide may accumulate in the respiratory centre and stimulate it to increase the ventilation. If the condition of the circulation becomes so poor that the amount of oxygen reaching the tissues is greatly reduced there will be incomplete combustion of the substances formed during cellular metabolism and the accumulation of acids in the blood. These acids, acting as a stimulus to the respiratory centre, will increase the pulmonary ventilation so that the carbon dioxide tension will be reduced and the oxygenation of the blood will be improved. Since the kidneys are normal the excretion of acid will go on rapidly, and as soon as the circulation has readjusted itself the excess of non-volatile acids will be got rid of. Then the alveolar air will return to normal. In cases with sufficient passive congestion, however, to inhibit the renal functions, there may well be some temporary retention of acids.

The second type of dyspneic patients consists of those in whom the element of acidosis plays a more significant part. Lewis recognizes that in this group renal lesions are generally present and believes that the acidosis is connected with nephritis, but he apparently feels that the evidence is as yet too scanty to allow of their being definitely associated together. Our own studies have been on cases in whom the renal condition has been investigated as carefully as possible. Blood-pressure, phthalein tests, and determinations of the non-protein nitrogen of the blood all support the view that these are usually cases with extensive degenerations of the kidneys. Clinically, the patients are frequently elderly persons, often with the pallor of arterial or renal disease, with comparatively little cyanosis. Orthopnea is present, and particularly characteristic are sudden attacks of severe dyspnea occurring especially at night. The respiration is usually rather rapid, shallow, irregular, and very frequently Cheyne-Stokes in character. The patients are often dull or sleepy, dosing off during the periods of apnea, arousing suddenly, and sometimes having great distress during the periods of dyspnea. The urine is that of chronic nephritis and the blood-pressure is usually well above normal. The condition is most often a permanent one, lasting days, weeks, and even months before death. Less often there are transient or fairly prolonged intervals of a return to comparative comfort and health. In general, the condition indicates serious organic disease and the prognosis is bad.

Analysis of the alveolar air in this clinical condition shows that

it is quite generally associated with a fall in the carbon dioxide tension. This decrease is not great, however, and the values, while sometimes reaching as low as 25 mm., are most frequently between 35 and 30 mm. In almost all the cases in which the symptom-complex has been clear cut and the acidosis evident the functional tests have shown that the kidneys were decidedly inefficient. Usually the phthalein output was measured as "traces" or "zero." It is thus quite natural, and probably correct, to conclude that the acidosis is due to an accumulation depending on incomplete excretion, and is of renal origin.

It is extremely difficult to decide how important a part the element of acidosis plays in producing the clinical symptoms of dyspnea in cardiorenal disease. In another clinical condition, such as diabetes, the same amount of acidosis as indicated by the alveolar air produces no gross changes in the respiration. In diabetes it is only when a much greater depression of the alveolar carbon dioxide has taken place that the breathing is affected, and even then a wholly different type of respiration results. The deep, regular respiration of diabetic acidosis is totally unlike the shallow rapid, irregular, periodic respiration of cardiorenal disease. If then the dyspnea of cardiorenal disease depends on acidosis alone it must be that there are other factors which modify the way in which the organism reacts. On the other hand, because the acidosis is not very great, one must not necessarily conclude that it is of no significance in the production of the dyspnea. Some observations recently finished indicate that it is of considerable importance.[23] Subjects have been allowed to breathe through valves attached to a so-called "closed-circuit apparatus." The expired air passes through two tanks and is subsequently rebreathed, so that the inspired air has a continually increasing content of carbon dioxide. By special arrangements the pulmonary ventilation of the subject is measured, and samples of the inspired air are taken at regular intervals for analysis. It has been found that normal individuals react in a fairly constant manner to the stimulus of the carbon dioxide in the inspired air. Thus when the carbon dioxide reaches a concentration of between 4.5 and 5.5 per cent. of the inspired air, the subjects are breathing so deeply that their initial ventilation has been doubled. Patients with cardiac disease, but who are compensated while at rest, react in a similar manner. Patients with decompensated cardiorenal disease, however, and with acidosis as indicated by the alveolar air, are much more sensitive to the carbon dioxide, and it is found that their ventilation may become doubled with only 2 or 3 per cent. carbon dioxide in the inspired air. It has already been shown that owing to the peculiar com-

[23] To be reported in detail in a separate communication.

position of the blood it can take up a great deal of acid without having its reaction perceptibly affected, but beyond a certain point, the mechanism fails, and the addition of even small amounts of acid affects the reaction noticeably. Here is the apparent condition in the patients with acidosis. The blood has already taken up all the acid it can without having its reaction affected, so that the addition of even small quantities, as in breathing the air containing carbon dioxide, makes a shift in the blood reaction and increases the pulmonary ventilation. The same result would undoubtedly be brought about if the carbon dioxide were produced in the body, as by muscular exercise. The amount of muscular work which would suffice to produce dyspnea would be much less than normal. Thus, while the degree of acidosis which is present in cardiorenal disease is usually insufficient to cause the changes in respiration which one is accustomed to associate with acidosis, or indeed to account for the dyspnea alone, it is undoubtedly an important element. It renders the organism unusually sensitive to any added production of acid, and would, in all probability, accentuate the effect on the respiration which might be produced by an inefficient heart.

HISTORICAL SKETCH OF THE DEVELOPMENT OF THE DUODENAL TUBE.[1]

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In connection with duodenal feeding let me sketch the development of the duodenal tube.

Shortly after the stomach pump was discovered by Kussmaul examination of the gastric contents became of great importance for the diagnosis of diseases of the stomach. As soon as physicians appreciated the value of the stomach tube it was felt it would be desirable to be able to examine also the secretion of the organs farther down, particularly the pancreas, because it was known the pancreas is of much greater value to the process of digestion than the stomach. But at first this wish—namely, to reach the secretion and analyze it—appeared to be impossible of fulfilment.

[1] Lecture delivered at the New York Post-Graduate Medical School, 1915.

For a number of years the first attempt to reach the pancreatic secretion was abandoned until Boas,[2] about 1889, published a paper in which he said that he had succeeded, by the introduction of a stomach tube into the fasting stomach and massaging the liver, in obtaining a fluid from the stomach which was regurgitated there from the duodenum. It gave the reaction of the pancreatic secretion. While it is possible, in rare instances, to succeed in bringing on such a regurgitation in the fasting condition, it is naturally not a procedure that can be done in a routine way. If there is, for instance, gastric juice in the stomach already the results will be vitiated.

The second step was undertaken by Boldyreff,[3] a Russian physician working in the laboratory of Professor Pawloff. He noticed on animals with gastric fistulæ that when they were given oil or fat a regurgitation from the duodenum into the stomach took place, and he suggested to make use of this phenomenon for clinical purposes. Volhard[4] then applied this test in practice. He gave oil or butter and half an hour later washed out the stomach. This method also is not applicable to all cases. In many regurgitation does not take place, or the regurgitated matter is mixed up with gastric juice, and is of no value.

Other more direct attempts have been made to obtain the duodenal secretion.

In 1897 Hemmeter[5] described a method by which he thought he could introduce instruments into the duodenum. A brief consideration of the construction of his instrument will make it clear that it is difficult to accomplish with this apparatus what Hemmeter claims.

Hemmeter's instrument consists of a rubber bag that resembles the stomach, and this bag contains in its upper segment a groove or a canal for another tube which is inserted into the duodenum through the pylorus as soon as the bag has been introduced and had been filled with air.

The trouble with this instrument is that stomachs vary in size and configuration. One can not obtain in advance a mould of any particular stomach, so that the bag will tally exactly with the shape of the stomach, and therefore it is impossible to say whether the opening of the groove in the bag is really opposite the pylorus. After the bag is in the tube is pushed down, and Hemmeter says

[2] Ueber Darmsaftgewinnung beim Menschen, Centralblatt f. klin. Med., 1889, No. 6, p. 97.

[3] Der Uebertritt des natürlichen Gemisches aus Pankreassaft, Darmsaft und Galle in den Magen, Pflüger's Arch. f. Physiol., 1908, p. 13.

[4] Ueber die Untersuchung des Pankreassaftes beim Menschen und eine Methode der quantitativen Trypsin bestimmung, Münch. med. Wchnschr., 1907, p. 403.

[5] Versuche über Intubation des Duodenums, Archiv f. Verdauungskr., 1897, Bd. 2, p. 85.

that he then succeeds in pushing the tube into the duodenum through the pylorus. I do not know, whether he succeeded or not. Hemmeter asserts that he obtained pancreatic secretion. This, however, is no proof that the secretion came from the duodenum through the tube, but I assume, rather, that he got it from the stomach. I do not believe it is easy to obtain pancreatic secretion by Hemmeter's instrument. The second clinician to try to reach the duodenum directly by means of instruments was Kuhn.[6] This was about one year later. He constructed tubes with a metal spiral inside. The spiral served to prevent too much bending and kinking and doubling upon itself. He then took a long stomach tube, put the metal spiral inside and manipulated it for a long time, until he thought he had reached the duodenum. He also maintained that he did get the pancreatic secretion. *X*-ray examination was not yet in vogue and so could not confirm the position of the tube in the duodenum. Kuhn's tube did not differ much from a stomach tube. I also experimented with it, but never succeeded in entering the duodenum with it. It certainly was a difficult procedure, both for the physician and for the patient. It is impractical.

After the publication of Kuhn's article Hemmeter gave up the use of the bag and tube and used Kuhn's instrument. This was the way things stood for a number of years. Then gradually I evolved the present instrument from various experiments and procedures that I will now give in detail.

I tried to find a method of testing the motor function of the intestines. For this purpose I[7] made use of porcelain beads, sifted the stool, and observed the time it took for them to reappear in the stool. This was described about eleven or twelve years ago.

Later, I desired not only to test the motor but also the digestive functions of the stomach and intestines. Various test substances (as meat, catgut, potato, fat, etc.) were attached to little beads.

The question now came up whether the digestion of the various test substances took place in the stomach or in the intestines.

In order to differentiate this,[8] I gave patients beads with test substances attached to a thread, arranged so that the thread was about 53 cm. long, so that the beads could not reach the duodenum. After four to five hours I pulled up the thread and looked whether the substance was still left. I worked with beads and thread so that the beads could not pass the pylorus. Thus I found which of the substances was digested entirely in the stomach. Those test substances which remained intact in the stomach but were missing

[6] Sondierungen am Magen, Pylorus und Duodenum des Menschen, Archiv f. Verdauungskr., 1898, p. 19.

[7] Diseases of the Intestine, 1904, 2d edition, p. 62.

[8] A New Method of Testing the Functions of the Digestive Apparatus, Med. Record, February 10, 1906.

on the beads when found in the feces must, therefore, have been digested beyond the stomach—in the intestine.

A short time later, while dealing with the question of the patency of the pylorus, I conceived the idea of giving beads to see whether they would pass the pylorus, in order to thus measure its permeability. This paper was published in 1908.[9]

The digestive test capsule as it is now made consists of the test substances all attached to beads, which again are held together by a silk string, the beads will reappear in the stool together, and we can then see which of the test substances have been digested and which have not.

In order to know whether the pylorus was permeable I had to have some substance which would change when it reached the duodenum and would not change in the stomach.

I attached to the thread one bead and a little bag containing a piece of dimethylamidoazobenzol-agar—the idea of using agar was to have a firmer substance than, for instance, test paper, so that the change of reaction should not take place too abruptly, but should proceed slowly.

Attach to the thread one bead at thirty inches from the lips, with dimethylamidoazobenzol agar, another one at twenty inches, likewise with dimethylamidoazobenzol agar, which latter can not reach the duodenum. The two beads are put in a gelatine capsule and given to the patient. Six hours later the beads are withdrawn and inspected. This should be done at a time when there is presumably free HCl present in the stomach, as for instance, one hour after Ewald's test breakfast. If the two beads are in the stomach, both will be red. If one was in the duodenum and one in the stomach the duodenal bead will be yellow and the other red. If we find that both are red, or that the lower one is red, we may suspect that there exists some obstruction at the pylorus to the passage of the beads from the stomach into the duodenum.

As soon as I noticed that we could enter the duodenum with the thread and the bead, I thought that it would be better to have a capsule or little bucket instead of the bead, as it could bring us the duodenal fluid itself.

That gave me the idea of the duodenal bucket (Fig. 1). If it is found that the bucket is filled with contents of an alkaline reaction containing pancreatic ferments, we know that we have been in the duodenum. Roentgen-rays confirmed that the duodenal bucket really was in the duodenum. This was described by me[10] in an article entitled "A New Method of Estimating the Permeability of the Pylorus and an Attempt at Testing the Pancreatitic Function Directly."

[9] A New Method of Estimating the Permeability of the Pylorus and an Attempt at Testing the Pancreatic Function Directly, New York Med. Jour., June 20, 1908.

[10] Loc. cit.

As soon as I saw that we could enter the duodenum with this instrument I had the desire to do something more for the pylorus or duodenum. I[11] constructed an instrument that could be pushed over the thread. This was a thin catheter, by means of which I obtained duodenal juice. The thread served as a guide to enter the duodenum. Not only can we aspirate the contents of the duodenum by the introduction of a catheter, but by means of another specially constructed instrument we can dilate the pylorus (October, 1909).

Taking into consideration that the introduction of this catheter instrument was not very agreeable to the patient, and that it could not enter deep into the duodenum, I soon afterward had the idea of employing simply a small rubber tube ending in a perforated

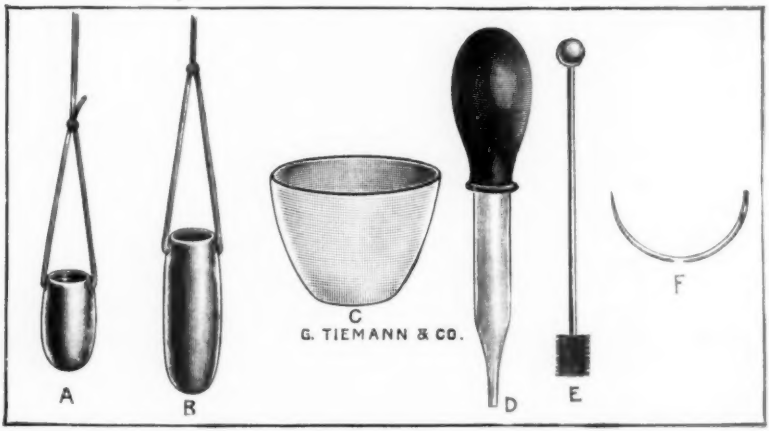

FIG. 1.—The duodenal bucket and its accessories. *A*, small size; *B*, larger size; *C*, porcelain dish; *D*, aspirating pipette; *E*, brush; *F*, needle.

metal capsule, which may be given instead of the bucket, letting the stomach do the work of introducing it into the duodenum. This is the main principle—instead of pushing an instrument to let the stomach carry out the work. This principle was of the greatest value. That led me to the construction of the duodenal pump, so-called because I first used it to aspirate the duodenal contents. It consists of a moderately thin rubber tube, at the end of which is attached a perforated olive. If the rubber tube is too thin, it is difficult to obtain the fluid; if too thick, it is too clumsy and not so pleasant for the patient.

[11] Max Einhorn, A New Method of Catheterizing the Pylorus and Duodenum, Medical Record, October 9, 1909.

This method was demonstrated by me[12] on a patient at the meeting of the Clinical Society of the Physicians of the German Hospital

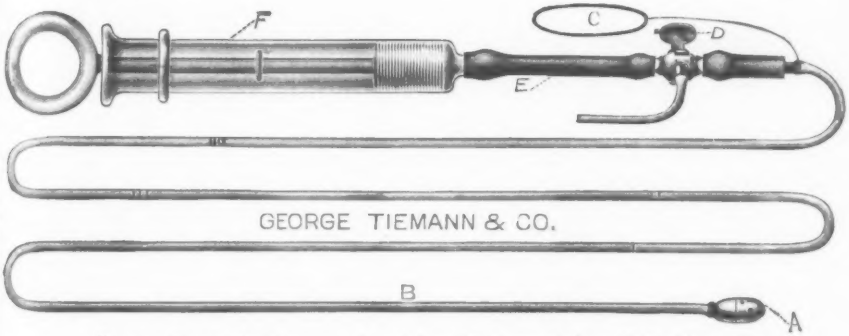

FIG. 2.—The duodenal pump. *A*, metal capsule, lower half provided with numerous holes, the upper half communicating with tube *B*: I, II, III are marks 40, 56, and 70 ctm. respectively from capsule; *C*, rubber band with silk attached to end of tubing, which can be placed over the ear of patient; *F*, aspirating syringe; *E*, collapsible connecting tube; *D*, three-way stopcock.

of New York, on November 11, 1909. There were about fifty practitioners present.

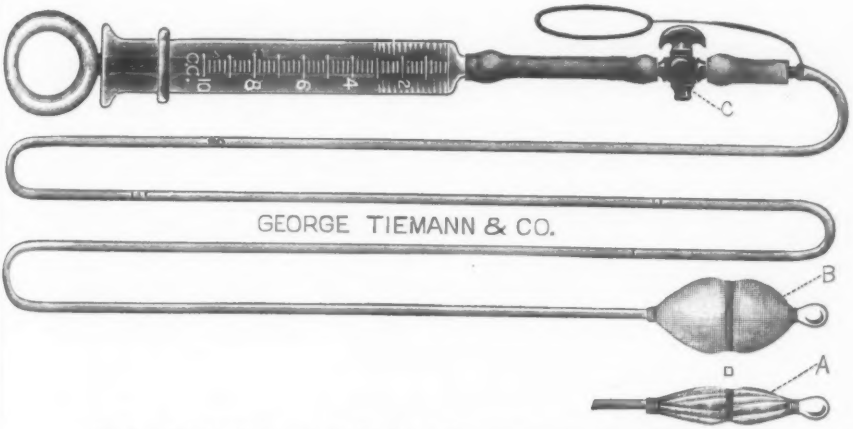

FIG. 3.—Pyloric dilator. *A*, rubber bag with gauze envelope in collapsed shape; *B*, rubber bag with gauze envelope, when inflated with air; *C*, stopcock.

As soon as I had the pump my desire was to treat obstruction of the pylorus without operation. There is a great deal of danger

[12] Max Einhorn, A Practical Method of Obtaining the Duodenal Contents in Man, Medical Record, January 15, 1910.

attached to operations on the pylorus. Extreme dilatation of the stomach is caused at times not so much by a real stricture, as by a spasm of the pylorus, as described by me and demonstrated at autopsy. There may be pyloropspasm without obstruction. I saw the good results obtained by stretching in cardiospasm and thought that similar results could be obtained in pylorospasm.[13] I constructed an instrument on a similar principle (Fig. 3).

The next point was that if we have the duodenal contents and can stretch the pylorus, we can also use the instrument for treatment.

One can now handle duodenal affections the same as gastric conditions.

FIG. 4.—Roentgen-ray photograph of patient K, with the Intestinal Delineator in the digestive tract, shortly after bismuth ingestion into the stomach. The course of the intestine is seen for about nine feet beyond the pylorus. I am indebted for this beautifully-executed Roentgen-ray photograph to Dr. W. H. Stewart, who took it for me at the German Hospital.

As soon as I had the duodenal pump, a physician consulted me, who was vomiting everything and could not be nourished by rectum, because of diarrhea. I used the tube for examination, and had the idea instead of taking out the tube, to leave it there and to employ it for nutritive purposes. I did so for ten days. He now feels well, having no trouble whatever. This was first done in December,

[13] Max Einhorn, Dilatation of the Stomach and Chronic Benign Ischochymia, Illinois Med. Jour., June, 1910.

1909. January, 1910, I[14] demonstrated this first patient with duodenal feedings before the Clinical Society of the German Hospital.

Now I will give you a few points by which to determine whether the tube is in the stomach or duodenum. If you aspirate and find that the fluid comes out quickly, looks watery, HCl present, Congo paper turns blue, dimethyl paper red, litmus paper red, then you know that it is in the stomach. If, on the contrary, you get only very little fluid, of neutral or alkaline reaction, and yellow color, then you know that you are in the duodenum. Sometimes a patient has no HCl in the gastric contents; how will you then know? There are two additional ways by which this may be determined: (1) by the way it is obtained, as shown by the extremely slow flow of the fluid, and (2) by giving the patient a colored liquid which he has not before had, either milk or raspberry syrup. Have the patient drink some milk and aspirate: if the milk is not obtained immediately after drinking it will be known that you are in the duodenum. To prove this still more conclusively, pull the tube up farther until you are in the stomach and then again aspirate, when you will obtain the milk that the patient has just swallowed. If the patient has had milk before the test, you can make use of raspberry syrup instead as an indicator. This test is more positive than an *x*-ray, but if desirable an *x*-ray may also be made.

How far can one go into the intestinal tract? I am grateful to Dr. McCafferty for consenting to have me test this on him. Now that the principle of allowing the natural forces to push the bucket along is recognized as correct, obviously there is no limit to letting it go as far as it wishes. The deepest I have gone is about nine feet beyond the pylorus. The deeper the bucket goes down the more, of course, the difficulty of pulling it up increases. I have an *x*-ray picture showing this (Fig. 4). We can undoubtedly enter still farther, only we must be careful that the tube does not curl up in the stomach.

We now have a clear conception of this instrument, and the new field it opens, in which one can study the pylorus, duodenum, gall-bladder, liver, pancreas, etc. I do not doubt that our advance in the study of digestive disorders will be most important along these lines.

[14] Max Einhorn, Duodenal Alimentation, Med. Record, July 16, 1910.

TONSILLAR ENDAMEBIASIS AND THYROID DISTURBANCES.

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A consideration of the literature on the causation of endemic goitre emphasizes very strongly the wide diversity of theories on this subject. The recent tendency has been leading away from the older chemical theories, and the idea of an infectious nature of the causative agents has been advanced. Specifically among such investigators, McCarrison[1] and Farrant[2] have, in the last two years, outlined a groundwork for the future studies on the bacterial toxic origin of thyroid overgrowth. McCarrison in a study of endemic goitre in India determined that the stools of goitrous subjects contained an infective agent by his ability to reproduce the clinical picture of goitre in test animals through the ingestion of this material. Raw water, particularly that containing slime from wells, etc., was held to be infected because of the production of goitre in men from a non-goitrous region when used by them. Boiling or filtering through a Berkefeld filter rendered the same water innocuous. He concluded from this evidence that a mineral substance is not the causative agent and that a bacterial origin is logical; and his results from the use of intestinal antiseptics add weight to the theory of an intestinal origin of the supposedly causative bacterial toxins. Farrant advanced the first definite evidence of a specific bacterial agent. In his earlier report, from his results of experimental inoculations and autopsies, he assigned various infections of the body to three groups in their relation to the thyroid: (*a*) those having no effect, (*b*) those that induce chronic or colloid goitre, and (*c*) those that produce complete or acute hyperplasia. It is only in Farrant's later work, however, that he proposes the theory and evidence of a mutant colon bacillus in the intestinal tract as an important factor in goitre production. The constant finding of this coliform bacillus led him to the belief that its prolonged ingestion in contaminated waters is a cause of endemic goitre through its production of a toxin which on absorption influences the thyroid. The suppurative streptococci and staphylococci, according to Farrant, fall into the group of non-

[1] London Lancet, January 18, 25 and February 8, 1913.
[2] British Med. Jour., February 28, 1914; ibid., July 18, 1914.

thyrotoxic bacteria, but Micrococcus catarrhalis is given a high place in the production of thyroid-stimulating toxins. As bearing upon the body of the present paper it may be mentioned here that while the location of the infection concerned in the production of such toxins is not an essential feature, Farrant is inclined to believe that pyorrheal conditions play a more important part in nature than do tonsillar infections.

Halstead,[3] in a reconsideration of the experimental side of the study of the relation of general and focal infections to thyroid enlargement, lays considerable emphasis upon infection being involved as a natural causative agent. Billings[4] urges a relationship between tonsillar focal infections and thyroid enlargement. Beebe[5] has made the relationship between pathological conditions of the nose and throat and hyperthyroidism the subject of a recent paper, in which attention is called to the fact that 40 per cent. of hyperthyroid patients in his experience give a history of repeated attacks of acute tonsillitis. He urges attention, likewise, to the care of upper respiratory conditions in the prevention of the subsequent development of hyperthyroidism. Norregard[6] reports an even higher grade of relationship, having uniformly found in a group of 35 thyroid cases some definitely infected lesion, usually in the tonsil. He refers to the anatomical relationship of the tonsils and thyroid in support of the suggested connection, and relates a complete recovery in one case after tonsillectomy, with improvement in other cases in which treatment was directed to similar conditions.

The interesting fact of the occurrence of acute thyroid hyperplasia in infants in Brazil (in the disease known as opilaçao) through the local infestment of the gland by a protozoan parasite, *Schizotrypanosoma cruzi* Chagas, which later proceeds into chronic goitre with cretinism if life persist, should be called to mind in the same general relation. It is true the recent work of Marine[7] and of Cannon, Binger, and Fitz[8] do not sustain this belief in the infectious origin of goitre, but neither in full sense eliminates the possibility of its importance. Marine in his more recent work on goitre in brook trout, following up the work of himself and Lenhart on this subject, fails to sustain the belief in its infectious origin; but concludes that in fish goitre is a non-infectious, non-contagious, symptomatic manifestation of a fault of nutrition, the exact biochemical nature of which is not known. In a series of feeding experiments a highly artificial diet of liver was apparently the major etiological factor, which could be corrected at once by the use of the whole sea fish as food. The kinetic theory of the causation of exophthalmic

[3] Amer. Jour. Med. Sci., January, 1914.
[4] Jour. Amer. Med. Assn., September 12, 1914.
[5] Ibid., August 29, 1914.
[6] Ugeskrift for Laeger, Copenhagen, January 14, 1915, lxxvii, No. 2, p. 51–74; abst. Jour. Amer. Med. Assoc., February 27, 1915.
[7] Jour. Exper. Med., January, 1914.
[8] Proc. Amer. Physiol. Soc., Amer. Jour. Physiol., March, 1915, p. 363.

goitre[9] would seem to receive additional weight from the experiments of Cannon, Binger, and Fitz, who, working on the theory that repeated emotional disturbance may lower a high neuron threshold and thus give rise to far more stimulation than normally, fused the anterior root of the right phrenic nerve of a cat with the right cervical sympathetic cord. With regeneration even the ordinary stimulus of normal breathing would stir up a volley of impulses in the superior cervical sympathetic ganglion. In the period from May to October, in four of six cats surviving operation they noted in one cat an increase from the normal 165 pulse beats per minute to 222, in others diarrhea and falling out of the hair of the neck and back, generally an unusual extreme excitability, and in one exophthalmos. In a word, by experimentally lowering a high neuron threshold in the sympathetic nervous system the typical picture of so-called exophthalmic goitre may be produced. From this study Jonnesco's work in the removal of the superior cervical sympathetic ganglion receives a degree of substantial support as an extreme surgical measure.

If the older classification of goitre be narrowed by the exclusion therefrom of enlargements of the thyroid gland which are of neoplastic nature and those dependent upon simple hyperemia, edema, hemorrhage, or upon suppurative changes, the remaining examples may be grouped in two classes: the first characterized by more or less active hyperplastic features of a simple or combined type, the second including chronic sclerotic, calcific, and atrophic parenchymatous changes as the main features (usually with accumulation of colloid in excess). While a relation between these two groups is by no means demonstrably clear, there are cases seen from time to time in which the sequence of early and progressive enlargement with symptoms of dysthyroidism into chronic enlargements with symptoms of hypothyroidism and with the type of histological changes of the chronic group is evident. It is theoretically conceivable that every case of chronic goitre has been preceded either by a frank stage of hyperplasia or by one of such gradual and insidious type that its clinical recognition has not been realized. It is at least permissible in our present uncertainty to tentatively adopt such view as a working theory, and to hold that in searching for a cause or for the causes of goitre the greater chance of success attends the close investigation of this supposedly constant but uncertain stage of active hyperplasia. Nor is it likely, when we appreciate that histological evidence indicates that the type of hyperplasia is not uniform, that the etiology is either simple or that the probable multiple causes are uniform in all cases. There are cases (the exophthalmic type) in which the hyperplasia concerns mainly, and to a marked extent, the lining cells of the follicles,

[9] Crile, AMER. JOUR. MED. SCI., January, 1913.

causing a moderate enlargement of the gland bulk, and a large occupation of the acinous spaces by the enlarged and multiplied cells at the expense of the ordinary colloid contents, and with changes in the appearance of this substance. On the other hand (parenchymatous goitres) the hyperplasia may in other instances involve the development of new acini and the enlargement of the existing ones with no important change in the size and appearance of the lining cells and with a general increase of the ordinarily appearing colloid. This latter form suggests strongly a true hypertrophy of the gland, such as would be called forth by some increased demand for its usual and full function. Or, as a third type, the hyperplasia may concern itself more particularly with the interglandular connective-tissue stroma, at times with and at other times without prominence of attendant vascular growth (leading into the fibrous and vascular goitres). In ordinary occurrences a given hyperplastic goitre may present any one of these types in predominance, or combination may be met with in which the histological pictures may vary among themselves and perhaps vary in different fields of observation of the same specimen.

If these variations are significant they argue best for the multiplicity of specifically operating causes, suggesting, on the one hand the likelihood of such examples of apparently pure hypertrophy as are seen in parenchymatous goitre, a general hyperplasia called forth by some demand for increased thyroid function, and, on the other hand, of stimulation to special cellular growth of the parenchyma (as in the exophthalmic type), of the connective-tissue framework (acute hyperplastic interstitial thyroiditis), or of the vessels (vascular goitres), by some selective agency operating directly upon these elements.

That special functional activity may be called forth indirectly, particularly in experimental conditions, by nervous stimulation is by no means inconceivable; and such an interpretation the writers are disposed to raise in explanation of the results of Cannon, Binger, and Fitz above referred to. (Here, too, one may conceive of the influence of emotion and of excess of sympathetic stimulation by hyperactivity of the adrenal and other chromaffin tissues.) All of our evidence of the purposes of thyroid function in life would indicate that it serves multiple objects in the economy, so that in selecting its undoubted but relatively poorly understood antitoxic or detoxifying importance in illustration of the argument the field of this line of consideration is by no means exhausted. We believe commonly that as an antitoxic organ the thyroid is efficient mainly through its iodothyrin secretion, probably largely by the iodin moiety of this molecule. One may well fancy, as has repeatedly been suggested, that some toxic substance (its precise character and its origin, whether inorganic or organic, whether exogenous or endogenous, being immaterial for the immediate

purposes of argument) which has a strong affinity for iodin may be constantly introduced into the economy from the ingested water or food or manufactured in the course of metabolism, or generated by microbic agencies here or there in the body; that such substance is, therefore, constantly robbing the economy of its iodin, and that in response the thyroid as the important iodin-secreting organ is called into particular activity to acquire and secrete iodin to replace this loss. Here might well fall the cases of apparent dietary fault (as those of Marine), or if there be a chemical fault in the water of *kropf-brunnen* (a view almost abandoned), it might well operate along such line; and here, too, if infection be, as is so frequently suggested, of importance one may be tempted to suspect that the toxins of the infection, irrespective of the site of the infection (only holding the likelihood of its persistence and of the continuity of toxin formation), may align themselves, having some special fixing ability of the iodin of the thyroid secretion and coming into contact with the latter either in the thyroid or in the general system as the case may be. Ordinarily the result of such a scheme should be a simple hypertrophy, but there can be for the present, at least, little ôbjection to the supposition that excessive demand might induce even the marked cellular hyperplasia of the exophthalmic type of goitre.

If, on the other hand, we admit the possibility of some selective stimulus to growth of one or other of the histological elements of the gland (notably, of course, the lining follicular cells), we at once should be disposed to attribute high prominence to agencies located in the gland or in such anatomical relation as to easily and in concentration arrive in the gland. This opens at once the infective possibilities and the local disturbances of surgical operation on the gland, recalling directly the possible involvement of the thyroid in opilaçao, the active cellular hyperplasia met in the remnants of the gland tissue when partial ablation of the thyroid is performed, and the variable hyperplasia met about foci of frank infection of the thyroid by suppurative bacteria. But there is no question of the usual rule of failures to demonstrate any type of microörganisms in the tissue of these hyperplastic thyroids, and one is disposed, therefore, to appeal strongly to the influence of toxins carried by as direct a route and in as concentrated quality as possible from extra-thyroid foci of infection to the gland. Here particularly may be assigned the frequent coincidence of various infective lesions of the mouth (pyorrhea), the tonsils, and the upper respiratory tract; the close lymphatic relation of the upper parts of the lateral lobes, as shown by Ehrhardt,[10] with the submaxillary and sublingual glands, being probably the route of admission of the supposed toxins to the organ. Stress has been laid more than once

[10] Beitr. z. klin. Chir., xxxi.

upon a relation between infections in the mouth and nose, and the writers present further evidence below of such relation; nevertheless, it should be emphasized that this cannot be regarded as excluding infections elsewhere from a similar relation (provided the toxins from that infection be thyroselective). Nor do the writers in the least care to be interpreted as holding goitre to be invariably the result of infection or the effect of infective toxins. But as one type of agency, either by calling out special thyroid activity or by direct selective stimulation to hyperplasia, infections or their toxins may perhaps be regarded as a factor in goitre production; along with nervous influences, the poisons of faulty alimentation and metabolism, as well as other possible factors. So far as the type of infection is concerned we would believe with Farrant that microörganisms (and their toxins) are in some degree selective, some not influencing the thyroid at all, others calling forth parenchymatous cellular growth and multiplication, still others inducing proliferation of the elements of the stroma, etc., and that in the matter of location no appropriate infection can be excluded; but the closer the focus and the more free and direct the mode of convection, the more pronounced and frank the effect is likely to be in the thyroid gland.

Several years ago some of us undertook a statistical study of endemic goitre in Wisconsin in connection with the work of the Medical Clinic in the University at Madison, with particular reference to evidence of its development in relation to preceding or coexistent infectious affections of the nose and throat.

Wisconsin's situation in the glacier zone with its geographical position in the goitre belt furnishes a fertile field for the study of endemic goitre. Some idea of the frequency of its occurrence can be gained from the following data obtained from the physical examinations of men and women entering the University of Wisconsin from 1910 to the fall of 1914 inclusive:

TABLE I.

Year.	Total examined.		Goitre.				Dysthyroidism.			
			Men.		Women.		Men.		Women.	
	Men.	Women.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
1910	819	512	140	17.1	217	42.3	4	0.5	2	0.4
1911	772	298	126	16.4	136	45.6	7	0.9	4	1.3
1912	1049	427	238	22.8	225	52.8	6	0.5	35	8.4
1913	1315	543	424	32.2	247	45.0	4	0.3	18	3.3
1914	1328	569	362	27.2	271	47.6	5	0.3	8	1.4

Taking the examinations of 1914, the following table (Table II) outlines the relative frequency of involvement of the different lobes of the thyroid in men, together with the pathological changes in the nose and throat found associated with these thyroid dis-

turbances. Of the 1328 men examined, 362, or 27.2 per cent., had thyroid involvement, and to this group the following figures pertain:

TABLE II.

		Cases.	Percentage.		
Simple goitre involvement	Both lobes and isthmus	169	46.6		
	Both lobes	38	10.4		
	One lobe and isthmus	42	11.6		
	Isthmus	57	15.7		
	Right lobe	34	9.3		
	Left lobe	17	4.6		
Dysthyroid involvement	Both lobes and isthmus	5	1.3		
	Total	362			
Pathological changes in nose and mouth	Nasal	80	22.0		
	Cryptic tonsils	6	1.6	22.8%	90.3%
	Cryptic and nasal	77	21.2		
	Fibroid and hypertrophied tonsils	25	6.9		
	Nasal, fibroid, and hypertrophied tonsils	140	38.6		

Without entering into a discussion of the details of this table a glance will impress the very marked prevalence of anatomical morbid changes in the tonsils and nasal passages in the group, a total of over 90 per cent. of the goitrous individuals showing such defects. It should be observed that only those changes which are resultant from a single long-continued or repeated inflammatory attack in the nose and throat are here included; and without possibility of histological classification the arrangement of the goitres has been simplified into two groups: those without symptoms or signs of thyroid intoxication being classed as simple goitres, and those showing undoubted constitutional symptoms of disturbed thyroid secretion as dysthyroid types.

The accumulated data of preceding years' investigation afforded decided evidence of the actuality of a connection between these nasal and throat affections and the large occurrence of thyroid involvement. The recognition of the tonsils as a site of parasitism by endameba gingivalis (Gros), in the laboratories of the Universities of Pennsylvania and Wisconsin raised the question of a possible connection of this organism with the thyroid enlargements in consonance with the evidence then attained of its importance in the etiology of pyorrhea and its probable importance in certain examples of chronic tonsillitis, and in various systemic complications, as arthritis, anemia, neuritis, etc.[11]

[11] Cf. Barrett, Dental Cosmos, August and December, 1914; Smith, Dental Cosmos, September, 1914; Bass and Johns, New Orleans Med. and Surg. Jour., November, 1914; Smith, Middleton, and Barrett, Jour. Amer. Med. Assn., December 14, 1914; Evans and Middleton, Jour. Am. Med. Assn., January 30, 1915 et al.

Two possibilities of etiological connection of these parasites with thyroid hyperplasia were considered: (*a*) direct extension of the protozoa from the mouth or nose or throat to the thyroid and parasitism of the organ by the amebæ, and (*b*) the effect of toxins arising from the symbiosis of the amebæ and their many bacterial associates upon the gland. The first was *a priori* held as improbable, because surely these organisms would long since have been detected in the course of histological study of early goitres. Nevertheless, a number of at least comparatively early specimens of hyperplastic goitres were examined with this point in view, without in any instance recognizing amebiform cells in the tissue. With the belief, however, that the second of these possible connections might be correct, a plan of study was projected and pursued.

The writers regret that, owing to the dominating thought of the importance of tonsillar involvement at first, this report fails to include pyorrhea as one of the sources of toxic substances suspected by them of being involved in thyroid complication of nose, mouth, and throat infections. This fault in reality, however, weakens only the statistics of coincidence and does not in any way militate against the force of the results reported. Moreover, in the future this may be easily, and probably with much profit, be corrected in certain work now in progress upon the general subject. Here, too, the writers are anxious for clarity to urge that in suggesting endamebiasis of these upper respiratory and mouth parts as one of a number of possible causes of thyroid hyperplasia they are not advancing these protozoa themselves as the specific producers of the toxins effective in producing the hyperplasia. If this were true there is no reason why everyone who is the host of these parasites (a high proportion of all adults) should not also be the subject of thyroid enlargement. Our belief is, that the essential toxic factors are really the products of the bacteria associated with the amebæ, and that these bacteria are the variants and the amebæ are the constants in many varying infections of the mouth, tonsils, and the nasal passages and sinuses; that there is a symbiotic relation between the protozoa and the bacteria, the amebæ by proteolysis of various cells producing a pabulum of special value for the nutrition and growth of the bacteria, and the bacteria being constantly ingested and digested by the amebæ; that as one particular form of bacteria is prominently present its toxin is liberated in prominent amount when the bacterial cells are thus digested; and that if that toxin has selective stimulative effect upon the thyroid elements, thyroid hyperplasia will follow (as following to Farrant, if there be a high proportion of Micrococcus catarrhalis present in the amebic lesion in the tonsils, for example, the toxin carried by lymphatic drainage into relation with the thyroid will stimulate the thyroid parenchymatous cells to growth and proliferation).

In prosecution of the study a series of 34 of the above (Table II)

goitre subjects with chronic cryptic tonsillitis were selected for further examination. Material was aspirated from the pouting crypts with a glass pipette bent toward the end and drawn out to a smooth point, a rubber bulb being attached. This material was mounted on a warmed slide, mixed with warm normal saline solution, covered, and examined immediately on the warm stage. Myriads of bacteria, spirilla, numerous granular leukocytes (pus cells), erythrocytes and a few epithelial cells constitute the ordinary findings. In 33 of the 34 cases examined, endameba gingivalis (Gros) was found present.[12] That in the course of this study 15 cases with chronic cryptic tonsillitis were also met with the same amebæ in the contents of the tonsillar crypts, but without thyroid enlargement is to our minds no indication, in the absence of knowledge of the bacterial associates with the amebæ in each individual case, that in the first group the thyroid changes were independent of the endamebiasis.

This group includes 25 individuals with simple goitre (11 women and 14 men) and 9 persons (5 women and 4 men) showing symptoms of dysthyroidism. In order to obtain some degree of evidence of a relationship amounting to more than mere coincidence between the tonsillar foci of symbiotic infestment and the thyroid changes, emetin hydrochloride was administered hypodermically to 23 of these 34 individuals. This mode of approach is, of course, an empiric one, and by no means ideal; but, as stated in a previous report,[13] "the application of a specific drug for the relief of a supposedly specific infection is an acknowledged therapeutic principle. The further application of this principle to the relief of remote conditions complicating the original specific lesion is justified." The general data of the entire group, with a statement of the thyroid involvement, the details of emetin treatment of 23 of the cases, and the results of such treatment, are presented in tabulated form for the sake of brevity in Table III.

The details of the administration of emetin hydrochloride were quite variable, that is, although the subcutaneous or intramuscular route was constantly used, the dosage and the number and the interval between the series of injections varied within rather wide limits. The period of observation ranged from two weeks to seven months. Reëxamination of the material from the tonsillar crypts after the use of emetin was made in but 16 of the 23 cases. Of these, in 13 reëxamination showed a disappearance of the endamebæ, a result in general conformity with the disappearance of tonsillar endamebæ previously noted by us[14] on the administra-

[12] Seven more cases of cryptic tonsillitis with thyroid involvement have shown endamebæ in the cryptal contents, bringing the total up to 40 positive cases out of 41 examined.

[13] Evans and Middleton, Jour. Amer. Med. Assn., January 30, 1915.

[14] Smith, Middleton, and Barret, supra cit.

TABLE III.

TABLE III.

No. and Sex.	Involvement.	Dysthyroid symptoms.	Tonsillar endamebæ.	Emetin hydrochloride treatment.	Time interval.	After treatment.		
						Amebæ.	Size of neck.	Symptoms.
1 M.	Right lobe	Tachycardia; tremor; nystagmus	+	3 series: 7, ½ gr.; 3, ½ gr.; 2, ½ gr.; 1, ½ gr.	5 mos.	+	Unchanged	Less nervous; no tremor; pulse fell from 96 to 84.
2 M.	Both lobes and isthmus	Exophthalmos, von Graefe, Moebius	+	1 series: 7, ½ gr.	1 mo.	+	Reduced ½″	(No goitre mass).
3 F.	Both lobes and isthmus	Tachycardia; fainting spells	+	3 series: 4, 1 gr. each	6 wks.	–	Reduced 1¼″	Psychic improvement.
4 M.	Both lobes and isthmus	None	+	None				
5 F.	Both lobes and isthmus	None	+	None				
6 M.	Both lobes and isthmus	None	+	None				
7 M.	Both lobes and isthmus, acute	None	+	2 series: 7, ½ gr.; 2, ½ gr.; 2, ½ gr.	5 mos.	–	Reduced ½″	
8 F.	Right lobe and isthmus	Exophthalmos; tremor; tachycardia	+	5 series: 2, ½ gr.; 2, ½ gr.; 2, ½ gr.; 2, ½ gr.; 3, ½ gr.; 4, ½ gr.; 4, ½ gr.	5 mos.	–	Reduced 1½″	Marked improvement in all symptoms.
9 M.	Left lobe and isthmus	None	+	1 series: 7, ½ gr.	3 wks.	–	Unchanged	
10 F.	Right lobe and isthmus	None	+	2 series: 4, 1 gr.; 4, ½ gr.	1 mo.	..	Reduced 1″	
11 M.	Both lobes and isthmus	None	+	1 series: 7, ½ gr.	1 mo.			
12 M.	Both lobes and isthmus	None	+	1 series: 7, ½ gr.	6 mos.	–	Reduced ½″	
13 M.	Both lobes and isthmus	Tachycardia; tremor; exophthalmos; von Graefe	+	None				
14 M.	Both lobes and isthmus	None	+	None				
14 M.	Both lobes and isthmus	None	+	None				
15 M.	Both lobes and isthmus	None	+	1 series: 7, ½ gr.	2 wks.	–	Reduced ½″	
16 F.	Both lobes and isthmus	None	+	3 series: 4, ½ gr.; 4, ½ gr.; 4, 1 gr.	6 wks.	–	Reduced ½″	
17 M.	Left lobe remains after operation	Atypical	+	2 series: 2, ½ gr.; 3, ½ gr.; 2, ½ gr.; 2, ½ gr.	5 wks.	?	Unchanged	Unimproved.
18 F.	Both lobes and isthmus	None	+	3 series: 4, ½ gr. each	6 wks.	–	Reduced ½″	
19 M.	Both lobes and isthmus	None	+	None				
20 M.	Both lobes and isthmus	Nervousness	+	3 series: 4, ½ gr. each	2 mos.	..	Reduced 1″	Unchanged.
21 F.	Both lobes and isthmus	Tremor; nervous; tachycardia	+	3 series: 2, 1 gr.; 4, ½ gr.; 3, 1 gr.; 2, 1 gr.	2 mos.	..	Unchanged	Marked improvement.
22 M.	Both lobes and isthmus	Tremor; fainting; lateral nystagmus	+	None				
23 F.	Both lobes and isthmus	Tachycardia; tremors; exophthalmos	+	None				
24 M.	Both lobes and isthmus	None	+	1 series: 7, ½ gr.	2 wks.	..	Reduced ½″	
25 M.	Both lobes and isthmus	None	+	1 series: 7, ½ gr.	4 mos.	–	Reduced ½″	
26 M.	Both lobes and isthmus	None	+	4 series: total, 6½ gr.	5 mos.	..	Reduced ½″	
27 F.	Isthmus	None	+	4 series: 4, ½ gr. each	2 mos.	..	Reduced ½″	
28 F.	Isthmus	Tremor; tachycardia; faint; exophthalmos	+	5 series: total, 7 gr.	4 mos.	–	Reduced ½″	Pulse fell from 120 to 88; improved in every way.
29 F.	Both lobes and isthmus	None	+	5 series: 7, ½ gr.; other 4, 4, ½ gr.	6 mos.	–	Reduced 1½″	
30 F.	Both lobes and isthmus	None	+	2 series: 4, ½ gr.	6 wks.	–	Reduced ½″	
31 F.	Both lobes and isthmus	None	+	5 series: total, 6+	7 mos.	–	Reduced 1″	
32 F.	Both lobes	None	+	None				
33 F.	Both lobes and isthmus	None	None	None				
34 F.	Both lobes and isthmus	None	+	None				

tion of emetin in certain arthritides complicating tonsillar endamebiasis. Twenty-two of the 23 treated have been under general observation since the beginning of treatment. Of these, 18 have shown a reduction in the circumference of the neck averaging about three-fourths of an inch (greatest reduction in Case 8, exophthalmic goitre, one and five-eighths inches; no reduction appreciated in 4 cases; in no case was there enlargement). Such changes in size of a goitre form, it is true, but a crude measurement of the influence of treatment; but the absence of fluctuations approaching or above their untreated state is to our minds more than of passing interest. Fluctuations are quite common among untreated cases, and fluctuations were met by us in 3 cases of goitre with acute upper respiratory infections under treatment in the group now under discussion, but in none was there any close approach to the condition existant before treatment. The measurements were made from a constant point just above the seventh cervical vertebra posteriorly around the neck over the most prominent point of the goitre mass anteriorly, in order to avoid error in the individual case. Seven of the 9 cases of dysthyroidism of the general group were included among the 23 cases treated with emetin, and showed varying degrees of improvement in their symptoms (in no case was there advance noted in the severity of the usual symptoms; in several the symptoms almost or quite disappeared under treatment, and have remained so). While precaution was constant to prevent psychic influence, this factor cannot be excluded in 3 of the cases. In fact, in no case was reference made to the real object of treatment except as an effort to clear up a tonsillar condition; the measurements of the neck and the changes in the size of the same were, with but few exceptions, treated as mere incidents.

In analysis of these results, which show primarily an extremely high proportion of positive finding of endamebæ in the tonsillar crypts in goitre subjects having, as is very frequently the case, chronic hypertrophic tonsillitis, and secondarily the frequent coincidence under treatment with emetin hydrochloride of (*a*) disappearance of the amebic parasites (with amelioration of the tonsillitis) and of (*b*) reduction in the size of the goitre and improvement in, or disappearance of, nervous and circulatory symptoms of dysthyroidism, brief attention should be further directed, perhaps, to the question of reduction in the goitre mass. The possibility of reduction to any degree must depend in the individual case upon the nature of the goitre. It could scarcely be expected in old fibroid or calcified goitres or in cystic goitres that the same degree of diminution in size could be attained (if any) as in goitres of recent enlargement closely connected with functionating excess. In the latter the removal of an exciting focus of toxin formation should be far more effective than in the former where permanent organic changes have been established; and in a general way the above tabulated results

indicate this in the more marked improvement met in the exophthalmic cases (as well in dysthyroidic symptoms as in the proportionate reduction in the goitre mass). From time to time, too, the question whether emetin does not possess a vasoconstricting action arises. Were this true it might be thought that reduction in the size of the goitre may, in part at least, be due to this factor. The rather ill-defined work of Muriel[15] reported early this year on the action of emetin constitutes the only assertion of such vasoconstricting influence of the drug as far as our present knowledge extends. Sollman,[16] on the other hand, attributes to the remedy a vasomotor paralyzing action, with fall of blood-pressure, in experimental animals; and all of the individuals in the present group whose blood-pressure has been followed (8) showed a very decided fall in both systolic and diastolic pressures. Studies now in course of completion at the University of Wisconsin on the vasomotor action of emetin hydrochloride under Dr. A. S. Lovenhart would indicate that the primary effect of the drug in test animals is a very transient vasoconstriction, succeeded by a definite dilatation of the vessels. Further studies with the plethysmograph on the effect of emetin hydrochloride on isolated organs are under way. From such data it would seem highly improbable that the reduction in the size of the goitres under observation by us could have resulted from a vasomotor influence of the remedy. Moreover, the uniformly maintained reduction over a number of months rather argues against so transient a matter as vascular constriction from vasomotor influence. We would prefer to believe, as above suggested, that the reduction noted in the goitre mass, as well as the amelioration of the dysthyroidic symptoms, is the result of the removal by emetin of the amebæ demonstrated in the tonsillar crypts in these cases, this resulting in a breaking of an important symbiotic chain of endamebæ and thyrotoxic bacteria, and removing thereby from these foci the active elaboration of the directly influential toxins. That absolute proof of this relationship is lacking we freely acknowledge, but believe there is more than mere suggestive value in the following conclusions which can be offered from the above.

Conclusions. 1. Tonsillar lesions of an infective cryptic character were found in 22.8 per cent.; and nasal together with tonsillar lesions existed in 90 per cent. of 362 goitrous individuals examined from this stand-point.

2. In typically diseased tonsils, out of 34 cases examined microscopically, 97 per cent. were found to harbor endameba gingivalis (Gros) in the tonsillar crypts.

3. Of 16 individuals of this group who after treatment by means of emetin hydrochloride were reëxamined, 13, or 81 per cent., were shown to no longer have endamebæ in the cryptal contents.

[15] Clinical Med., February 1, 1915.
[16] Text-book of Pharmacology, ed. 1906, p. 309.

4. In 23 individuals to whom emetin was administered a reduction in the bulk of the goitre was appreciable in 18 individuals; and of 7 dysthyroid cases included in this group of treated cases 6 were benefited in degrees varying from slight amelioration to apparent cure.

5. Inability to demonstrate endamebæ in the thyroid gland renders improbable any direct causal relation of the amebic infestment of the tonsils *per se* upon the development of thyroid disturbances.

6. However, the improvement, morphologically and symptomatically, in the treated cases leaves little doubt, after ruling out a vasomotor influence from the emetin employed, as to an indirect relationship. A symbiosis of endamebæ with appropriate bacteria, leading to the elaboration and absorption into the thyroid of selective thyrotoxic poisons, is at least conceivable in explanation of such relation.

7. In no sense do the writers care to be understood as advancing hereby an exclusive explanation for all goitres; other types and other locations of infections capable of producing thyrotoxic toxins, perhaps, too, toxic substances having a similar influence but derived from metabolic or alimentary fault, or even entering the body from without, are all of possible influence; nor is the influence of sympathetic stimulation, however accomplished, to be overlooked. The writers are unable to follow, moreover, in any of these lines of thought, into any satisfactory explanation of the known occurrence of belts of endemic goitre along certain well-defined glacier drifts.

We desire to express our appreciation to Doctor R. H. Jackson, of Madison, for gross specimen of goitre and to Doctors Van Valzah, Rinker, and Morris, of the clinical staff of the University of Wisconsin, for kind coöperation in this study.

PATHOGNOMONIC ALTERATIONS OF THE CEREBROSPINAL FLUID IN SYPHILIS OF THE NERVOUS SYSTEM.[1]

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The cerebrospinal fluid of healthy individuals has a fairly constant constitution. Although we do not know its origin or its functions, we know that it is subject to alteration of constitution in many diseases, and especially in diseases of the central nervous system. Much study has been made to determine the specificity of such

[1] Read at the Meeting of the Association of American Physicians, Washington, D. C., May, 1915.

alteration—that is, whether there occur pathognomonic alterations of the cerebrospinal fluid. It need not necessarily show abnormality in any disease. It is usually altered in disease of the central nervous system, caused by pathogenic organisms (Diplococcus intracellularis, tubercle bacillus, poliomyelitis organism, Treponema pallida, etc.). It is most constantly altered in syphilitic diseases of the central nervous system. In the majority of such diseases, it is altered in a characteristic way, and in some the alteration is so constant and unvarying that it may be considered pathognomonic. When the syphilitic disease of the central nervous system is predominantly of the meninges and bloodvessels, that is, when the brunt of the lesion is borne by the connective-tissue structures, the change in the cerebrospinal fluid is subject to wide variation, depending upon the intensity of the infection, the rapidity and extent of the pathological process, and upon the individual (vital resistance).

Meningeal Syphilis, Cerebrospinal Syphilis. When the pathological process is confined largely to the meninges, the circumvascular spaces, and the bloodvessels the most conspicuous alteration in the cerebrospinal fluid in addition to the positive Wassermann reaction is an increase of the cellular elements of the fluid and particularly an increase of the mononuclear cells. If this increase amounts to 100 or more the cubic millimeter, and the polynuclear variety of cells are above 10 per cent., it may be assumed with much confidence that the syphilitic process is predominantly meningeal, it matters not what the clinical display is. If the fluid with these characteristics does not reduce Fehling's solution and shows no excess of globulin the assumption is even more certain. Furthermore, it is likely that such cases will yield promptly to appropriate treatment, inasmuch as the pathological alteration in the cerebrospinal fluid can be quickly brought, approximately, to a normal state. Of a large number of cases to bear out these statements I quote two:

Case I.—Female, thirty-eight years old; married. There is no history of syphilitic infection; she has borne three children and four miscarriages. Complaint: breaking pains in arms and legs, headache, insomnia, nausea, occasional vomiting, indigestion, constipation. Duration of symptoms, eighteen months. Has been constantly under treatment for dyspepsia.

Physical Signs. Liveliness of the tendon-jerk; tremor of the outstretched fingers and of the lips.

	Sept. 2, 1912.	Sept. 16, 1912.	Nov. 20, 1912.
Serum, Wassermann	+	+	−
Cerebrospinal fluid, Wassermann	+	+	−
Cells (180 polynuclears)	1480	149	5
Globulin	+	+	−
Fehling's	+	+	+

CASE II.—Male, aged twenty-six years; unmarried; became infected with syphilis one month before he consulted me for the relief of headache, spasm of the left side of the face and left upper extremity, lethargy, stuporousness, dysarthria, and anarthria. The evolution of these symptoms occurred in three months. Physical examination was negative, save for a slight paresis of the motor branch of the right fifth and of the seventh cranial nerves. Laboratory examinations.

	Oct. 7, 1913.	Oct. 20, 1913.	Oct. 31, 1913.	Dec. 9, 1913.	Dec. 22, 1913.	Mar. 17, 1914.	June 5, 1914.
Serum, Wassermann	++	+	−	+	−	−	−
Cerebrospinal fluid, Wassermann	+	+	+	+	−	−	
Cells (12 polymorphonuclears)	533	171	70	34	16	12	5
Globulin	+	+	−	+	−	−	−
Fehling's	+	+	+	+	+	+	+

He received nine intravenous injections of salvarsan within two months and was then given salicylate of mercury hypodermically.

THE SEROLOGY OF ONE HUNDRED AND SEVENTEEN CONSECUTIVE CASES OF CEREBROSPINAL SYPHILIS. Examination of the blood serum of patients with that form of syphilis of the nervous system in which the brunt of the lesion is borne by the connective tissues of the central nervous system, shows that the Wassermann reaction in the blood serum is positive in 88 out of the 117 cases; the cerebrospinal fluid Wassermann is positive in 33 cases; and there is an excess of globulin in 46 cases. The cases were distributed as follows:

Serum (Wassermann).	Cerebrospinal fluid (Wassermann).	Globulin cases.		
+	+	+	23	
+	+	−	6	
−	+	+	3	
−	+	−	1	
			—	33
+	−	−	46	
+	−	+	13	
−	−	+	7	
−	−	−	18	
			—	84

Forty-six of the 117 show a positive Wassermann in the serum and a negative cerebrospinal fluid with a normal cell count.

In 23 of these cases no cells were found, in 16 not over ten cells, in 4 not over twenty cells, while 2 cases had a cell count between twenty and thirty cells.

The next largest group of cases—namely, 23—is that in which the serology is positive throughout and in which there is either a moderate or a marked pleocytosis; 11 of these 23 cases had a cell count of more than one hundred, while it ranged between ten and eighty cells in 12 cases; 2 of these cases showed the largest cell count obtained in any of the cases, namely, 1882 and 1630 respectively.

In 18 of the total of 117 cases the serology was negative throughout. In 5 of these cases there were no cells: in 8 between ten and twenty cells, and in the remaining 5 the cell count ranged between thirty and one hundred and fifty. In 13 of the total number of cases the serum Wassermann and the globulin were positive, while the Wassermann in the cerebrospinal fluid was negative. In this group of cases a moderate pleocytosis is the rule: 1 case had no cells, 3 not over ten, 2 not over twenty, 3 not over thirty, 2 between thirty and fifty, while 2 cases have over one hundred and two hundred cells respectively.

In 7 cases positive globulin was the only positive serological finding; while in this group the cell count ranged between ten and fifty cells, there was 1 case which showed over two hundred cells. In 6 cases both the serum Wassermann and that of the cerebrospinal fluid was positive, while the globulin test was negative. Only 1 of these cases had more than ten cells. In 3 cases the serum Wassermann was negative, while that of the cerebrospinal fluid and the globulin was positive; 1 of these cases had not more than ten and 2 not more than thirty cells. In 1 case only was the Wassermann of the cerebrospinal fluid the only positive feature of the serology. The cell count was not over fifty.

The Cerebrospinal Fluid in Tabes. The cerebrospinal fluid taken from individuals whose brain and spinal cord display the reactions to the Treponema pallida that are known as general paresis and tabes is characteristically altered in from 60 to 75 per cent. of them.

The typical serological picture of tabes is: serum, Wassermann, +; cerebrospinal fluid, Wassermann, +; cells, 20 to 100; globulin, − + (usually −); Fehling's, +.

Increase of lymphocytes is the most constant alteration of the cerebrospinal fluid of individuals with tabes. In 200 consecutive cases, 154 had cellular abnormality of the fluid. In 30 instances the number of cells to the cubic millimeter of fluid was under five, and in 16 of these there were no cells. Of the 154 cases there were 23 which had upward of one hundred cells to the cubic millimeter. Such cases we are accustomed to designate hyperlymphocytic tabes, and we have learned that they are more amenable to treatment than the hypolymphocytic varieties. Polynuclear elements in the spinal fluid of this variety of tabes is the exception, not the rule. The highest count in any patient of the two hundred consecutive cases was 592. There were 50 instances in which the count was about sixty and 122 instances in which it was about twenty-five.

We have never observed a case of hyperlymphocytic tabes with one thousand cells to the cubic millimeter in the spinal fluid. The extreme limit of the pleocytosis observed is well within four hundred cells per cubic millimeter. The presence of polynuclear elements in the spinal fluid of this variety of tabes is rather the exception

than the rule. Whenever found this phenomena is to be considered of favorable prognosis. It must be emphasized at this junction that the irritation is responsible for the pleocytosis, whereas the spirochete *per se* is responsible for the positive Wassermann reaction. The one may be removed without in the least influencing the latter, so that we may therapeutically succeed in doing away with most, if not all, of the pleocytosis, leaving behind a Wassermann reaction which cannot be influenced under any circumstances. Such a case is the following in this communication.

So-called Wassermann-fast Cases. A gentleman, aged forty-seven years, recalled when his recollection was refreshed, that when a youth he had preputial ulceration of some sort to which he gave no attention. Four months before consulting me he experienced a sensation of heaviness in the feet and legs and occasional shooting pains. His complaint when I saw him was: weakness of the legs and some awkardness in his walking; cushion sensation under the balls of the feet, numbness in the peroneal region; occasional imperative desire to urinate. His physical signs were typical of tabes: serum, Wassermann, +; cerebrospinal fluid, Wassermann, +; cells, 98; globulin, −; Fehling's, +.

From October, 1910, he received 18 injections of salvarsan, 24 injections of neosalvarsan, 5 injections of salvarsanized serum, and 46 injections of salicylate of mercury.

The serum Wassermann test made once a month remained positive up to May 29, 1915, when it was found negative for the first time and the cerebrospinal fluid was likewise entirely negative. His symptoms at this time practically disappeared and he was discharging the obligations of an exacting professional duty, that of a general practitioner of medicine. On August 7, 1915, the serum Wassermann was again +.

Out of the 200 cases there were 7 instances in which it was impossible to make the serum negative despite the most protracted administration of antisyphilitics.

One of the most extraordinary and inexplicable occurrences is the behavior of the cells in the cerebrospinal fluid in certain cases of tabes in active treatment. In several instances (the percentage of cases is not yet ready to report) the cells of the cerebrospinal fluid increase while the patient is having very active antisyphilitic treatment. I publish the serological card of one patient to illustrate this:

	Serum (Wassermann).	Cerebrospinal fluid (Wassermann).	Ce'ls.	Globulin.	Fehling's.
May 3, 1915	+	+	1	−	+
May 27, 1915	+	−	12	−	+
July 8, 1915	+	+	3	−	+
Aug. 12, 1915	+	−	3	−	+
Oct. 18, 1915	−	+	20	−	+
Nov. 11, 1915	+−	+	14	−	+
Nov. 23, 1915	+	+	6	−	+
Dec. 8, 1915	+	+−	270	−	+

In the interval that elapsed between the first day given above and the last, he received eight intravenous treatments of salvarsan, three intraspinous treatments of mercury, and eighteen intramuscular injections of mercury salicylate.

Clinically the patient made very striking improvement; from being absolutely bedridden, he was able to get about the hospital without other aid than that of a stick, and the pains, of which he previously complained bitterly, had practically disappeared.

The cerebrospinal fluid taken from individuals who have tabes reduce Fehling's solution in nearly every instance. In 12 cases only out of 200 consecutive cases did it fail to do so.

The globulin of the cerebrospinal fluid is increased in nearly 50 per cent. of the cases. So far I have not been able to associate the increase of globulin with any definite clinical type of tabes.

When studying the blood serum and cerebrospinal fluid of patients who have disease flowing from syphilis it is of the greatest importance to determine whether the patient has recently taken treatment that is known to deter the Wassermann reaction. I have gone through the histories of my cases with much care to determine this; 41 of the 63 cases whose serum gave a negative reaction had received mercury or salvarsan before coming under my observation; 22 of them had not.

Of the 27 patients whose Wassermann reaction of the cerebrospinal fluid was negative, 17 had received antisyphilitic treatment.

TABES AND KNOWLEDGE OF SYPHILITIC INFECTION. A study of these 200 cases of tabes throws interesting light on the incidence of tabes. The accompanying table sets this forth:

Males	161	
Females	39	
		200
History of infection—hard chancre	108	
Soft chancre	13	
Gonorrhea	20	
	141	
Denied	59	
		200
Treatment at the time of infection	107	
No treatment	93	
		200
Treatment later	102	
No treatment later	98	
		200

THE SEROLOGY OF GENERAL PARESIS. In 70 consecutive patients afflicted with general paresis, the majority of them in the early stage of the disease, and 58 of which were males and 12 females, the Wassermann reaction of the serum was positive in 47 instances, negative in 17, and refused or not recorded in 6.

The Wassermann reaction of the cerebrospinal fluid was positive

in 53 instances, negative in 7 instances, and refused or not recorded in 10 instances.

The cerebrospinal fluid showed an increase of the cellular elements beyond the normal in 52 instances, no increase in 9, and no record in 9. The highest cell count of any case was two hundred and seventy. There were 9 instances in which the pleocytosis was above one hundred and 16 instances in which it was above fifty. The average cell count was fifty-eight, though the majority of instances showed a pleocytosis of from thirty to fifty.

The globulin of the cerebrospinal fluid was increased in 45 instances, not increased in 15, and no record in 10.

The characteristic precipitation of colloidal gold occurred in 97 per cent. of the cases of paresis. It will be recalled that Szygmondi suggested the use of colloidal metals to determine the quality of protein substances, and Lange attempted to determine the nature of the protein substance in the cerebrospinal fluid by an elaborate series of experiments with colloidal gold. It is not apparent, however, in the work of Lange that he came to any definite conclusion concerning the nature of the protein in the spinal fluid. The precipitation that he obtained with the use of colloidal gold suggested to him that it would be of great value in detecting syphilis. We were unable to corroborate the claim that colloidal gold, used after the manner described by Lange, is to be depended upon as a detector of syphilis in general, but it is the most reliable and unvarying phenomenon of general paresis.

The Effect of Treatment upon the Alteration of the Cerebrospinal Fluid in Paresis. It goes without saying that the denial of syphilitic infection on the part of the patient who has general paresis has very little weight. In this series of cases it was admitted in 29 cases, denied in 25, and nothing known of such an occurrence in 13.

The results of treatment may be summarized in a sentence; although the constitution of the cerebrospinal fluid is modified in many instances by the administration of salvarsan and mercury, it was never made normal.

Conclusions. *Cerebrospinal syphilis* (lesion predominantly of the meninges, bloodvessels). The blood serum gives a positive reaction (if the patient has not been subjected to antisyphilitic treatment) in about 75 per cent. of the cases.

The cerebrospinal fluid, on the other hand, gives a positive Wassermann reaction in only about 30 per cent.

The most constant alteration is pleocytosis. It occurs in upward of 80 per cent. of the cases. In the vast majority of instances the cell count is less than 100 to the cubic millimeter, though it may be more than 2000. Although treatment (salvarsan, mercury) usually reduces the number of cells, it does not always do so. Occasionally the pleocytosis increased within forty-eight hours after treat-

ment. The predominating cell is the mononuclear, but the higher the cell count the greater the admixture of polynuclear elements.

The globulin content of the fluid is increased in about 45 per cent. of the cases.

The fluid of patients with cerebrospinal syphilis reduces Fehling's solution in about 95 per cent. of the cases, but this has practically no diagnostic value, as the fluid taken from patients who have any organic nervous disease does the same thing. When a fluid does not reduce Fehling's it will be usually found to contain a large proportion of polynuclear cells.

Tabes. Lymphocytosis is the most constant alteration of the spinal fluid (75 per cent.). The number of lymphocytes in some instances suddenly increases while the patient is under active treatment.

The next most constant alteration is a + Wassermann (73 per cent.). The globulin is increased in 50 per cent. of the cases.

General Paresis. The cerebrospinal fluid gives a + reaction in 80 to 85 per cent. of the cases; an increase of the cellular elements in practically the same percentage and globulin increase in about 65 per cent.

The colloidal gold test is positive in 97 per cent. of the cases.

SPONTANEOUS PNEUMOTHORAX.

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Pneumothorax is always secondary to disease of the lungs or of the chest wall, and therefore is a complication and never a primary condition. As a rule the disease to which it is secondary is obvious, but occasionally the pneumothorax dominates the clinical picture and the primary condition is obscure and in a measure unimportant. Pneumothorax occurring when the lungs are relatively healthy may cause such trivial symptoms as to be entirely unsuspected and its presence be revealed in the course of a routine examination. Although the physical signs of pneumothorax are straightforward enough, still if one is off guard they may be overlooked or misinterpreted.

My own experience with pneumothorax, until I made the observations herein recorded, had been gained by encountering it in cases with gross and obvious pulmonary disease or after injury to the chest wall. In these instances the symptoms were marked and the physical signs, though interesting, still were quite clear and direct in their significance. I was unprepared, therefore, for the following observation, which aroused a keen interest:

CASE I.—*A young man during a cold has sudden pain in the right side. A few days later, December 2, 1909, examination reveals a complete right pneumothorax. Uneventful recovery in six weeks. On November 4, 1910, after lifting a weight, pain in the left side. Examination reveals complete left pneumothorax. Uneventful recovery in four weeks. Recurrence of left pneumothorax on December 24, 1910. In October, 1913, cough, sputum, signs of tuberculous infiltration in both upper lobes; tubercle bacilli in sputum.*

Dispensary No. 5074. A. G., white male, aged twenty-two years, elevator constructor, came to the Phipps Dispensary of the Johns Hopkins Hospital on November 12, 1909, complaining of cough and pain in the lower right side. His father had been killed in an accident, his mother was living and well. He had four brothers and one sister all living and well; no history of tuberculosis in the family.

Patient had always been a healthy man and had had no serious illness since childhood. He had been a hard worker, smoked moderately, and did not abuse alcohol. He had had a cough for two years, dating his illness from a cold which he had contracted at that time. He had never had any constitutional symptoms. A few weeks before coming to the hospital he had contracted a fresh cold, and since then his cough had been worse, and he had had some pain in the right side. His average weight had been 123 pounds. On admission the temperature was 98.2°; pulse 72; respirations 22; weight, 130½ pounds; height, 5 feet 5¾ inches. The note of the examination on admission is as follows:

Patient is a well-nourished man of healthy appearance; his skin is rather pale, but the mucous membranes are good color. Tongue is slightly coated; teeth are in bad condition and there is definite pyorrhea. The mucous membranes of the throat are reddened and the left tonsil somewhat enlarged. The cervical glands are palpable, but are not particularly enlarged. There is no general glandular enlargement. The chest is well formed, right clavicle a little more prominent than the left; movement somewhat restricted over the right side. Tactile fremitus well felt on both sides, more marked on the right than on the left. The percussion note is a little impaired above and below the right clavicle and in the supraspinous fossa and at the extreme base. A few fine rales and an occasional medium moist rale heard over the area of impairment. Heart: the point of maximum impulse is in the fifth interspace, inside the nipple line; sounds are clear. Abdominal examination shows nothing noteworthy.

December 4, 1909. Patient felt well until the afternoon of November 28, when upon stooping over he suddenly experienced a sharp pain in the right side, followed by shortness of breath The shortness of breath was not urgent, but he could not walk a block without stopping to catch his breath. Since then he has had pain in the side constantly and is unable to lie on his back or on the right

side on account of the pain. The shortness of breath has continued but occurs only upon exertion.

December 2. It was noticed that the breath sounds were absent over the right side, but the examination on that date was incomplete and the true condition was not made out.

Examination.—The patient is perfectly comfortable and walks about the dispensary without the least sign of distress. Pulse 90, respirations 20. The chest well formed and fairly symmetrical; both clavicles are prominent, the right perhaps a little more so than the left; movement about equal on the two sides, a little less on the right, but the difference is not striking. Fremitus is better felt over the upper right back than on the left side, but elsewhere, though felt, is distinctly diminished as compared with the left. The percussion note is a little impaired above and below the right clavicle and in the interscapular area. Over the lower front, and particularly below the angle of the scapula, the note has a distinct hyperresonant quality. On the left the lower border of the lung, in the midaxillary line, gives an excursion of 6 cm. on deep inspiration. On the right the lower border of resonance extends to the level reached by the lung on the left on full inspiration, and this point shows no respiratory variation. When the patient lies down the hyperresonant quality of the percussion note over the front is still more marked than when he sits up. On auscultation the striking feature is the suppression of the breath sounds. They are everywhere audible, but very distant and faint. The voice sounds are somewhat diminished in intensity, but show no alteration in quality. The point of maximum impulse is in the sixth interspace outside the mammillary line, and there is no cardiac dulness to the right of the sternum; heart sounds are clear. The roentgenogram shows a complete right-sided pneumothorax, with marked dislocation of the mediastinum. The tuberculin tests—1 per cent. and 5 per cent.—conjunctival, and cutaneous tests are all negative; the sputum shows no tubercle bacilli.

December 14. Patient has been feeling much better; he has no pain now and can lie with comfort on the right side. He walks with little discomfort; he has a little cough and expectoration. Examination shows the point of maximum impulse to be distinctly farther to the right, in the sixth interspace, just inside the mammillary line, 8 cm. from the median line. The percussion note is not so hyperresonant as before; indeed, there is little difference in the note on the two sides. Fremitus is almost as well felt on the right as on the left side. The lower border of the right lung moves 3 cm. on deep inspiration in the midaxillary line. The breath sounds, though distant, are better heard than on the previous examination. The whispered voice sounds have a distant bronchial quality. The deep inspiration following cough is accompanied by numerous fine moist rales heard over the whole front. Roentgenogram shows that the right lung is beginning to expand.

December 31. Patient now feels well and is anxious to return to work. He has taken his temperature regularly during the past month, and it has never been over 99°. His pulse has been around 90. He still has a little pain in the chest when he stoops over. Examination now shows the percussion note to be resonant over the right side, with a little impairment above and below the clavicle and in the upper interscapular area. Breath sounds are vesicular and distinctly heard over the whole side, although not as loud as on the left. A few coarse, moist rales are heard on deep inspiration. The lower border of the lung moves 6 cm. on deep inspiration in the midaxillary line. The point of maximum impulse is in the fifth interspace, 7.5 cm. from the median line. The roentgenogram shows that the lung has completely expanded. There is marked increase in the mediastinal shadows and of the radiating bands to both upper lobes, particularly to the right. Three sputum examinations have been negative for tubercle bacilli.

November 8, 1910. Patient returns to the dispensary saying that on November 4, after lifting a weight, he suddenly experienced pain in the left chest. Since then he has had some pain in the side, but he has practically no shortness of breath or other discomfort.

Examination. Patient looks comfortable; there is no dyspnea. Pulse and respirations not increased in rate. The left side of the chest is fuller than the right, although there is little movement seen on the left side. The note over the left chest is hyperresonant, but not markedly so. There is practically no cardiac dulness to the left of the sternum. Breath sounds on the left side are almost entirely absent. On the right they are loud and harsh. On the right the lower border of pulmonary resonance descends 6 cm. on full inspiration. On the left resonance extends to the same level as resonance on the right in full inspiration and this point does not change on inspiration and expiration. Litten's sign is well seen on the right; it is absent on the left. Roentgenogram shows a definite pneumothorax on the left side. The upper lobe is only partially collapsed; the lower lobe more markedly; there is moderate displacement of the heart to the right.

November 23. Patient has been feeling well, and has had practically no dyspnea. Percussion note is now resonant on both sides and the breath sounds heard with normal intensity over the left. The roentgenogram shows that the lung has completely expanded and that the heart has returned to its normal position.

December 10. Has felt perfectly well except that he caught a cold last week and has had some pain, generally distributed over the chest. At present he has considerable cough and a little morning expectoration. He thinks the expectoration comes mainly from the nose. A sputum examination has been negative.

Examination. Patient looks well; the lips and nose are a little blue, but the morning is cold. The right clavicle is a little more

prominent than the left, and the right shoulder droops a little. The left shoulder moves a little more freely than the right; the lower part of the right chest moves a little more freely than the left. The note is everywhere resonant, except there is a little impairment above and below the right clavicle and in the right supraspinous fossa. The lower border of the lung in the midaxillary line moves 6 cm. on the right and 5 cm. on the left on full inspiration. Fremitus is everywhere well felt, somewhat better on the right than on the left side. The breath sounds are everywhere loud and vesicular, rather harsh over the right upper lobe. The point of maximum impulse is in the fifth interspace just inside the mammillary line; there is a normal area of cardiac dulness.

December 27. Patient returns, stating that on the evening of December 24, while sitting quietly in a chair, he was taken suddenly with a sense of discomfort in the left side, which gradually increased in severity, particularly when he attempted to lie down. At present he has no pain except when he stoops over. On walking fast he has some pain in the left side and is a little short of breath, otherwise he has no dyspnea.

Examination. The patient looks well. The left side is more prominent than the right; it moves with respiration, but less than the right. The left chest is hyperresonant throughout. Fremitus is absent on the left side, and the breath sounds are absent except in the interscapular area, where they are very distant, and have a slight amphoric quality. The point of maximum impulse is seen just to the left of the lower end of the sternum. The roentgenogram shows a well-marked pneumothorax on the left side, with marked dislocation of the mediastinum to the right. The lung is generally although not completely collapsed.

January 14, 1911. Patient has been feeling quite well, although the cough has at times been troublesome. He has had very little shortness of breath except when he attempts to walk rapidly. He has no pain in the chest except on lying down. He has taken his temperature regularly during the past two months, and it has never been over 99°. Pulse ranges from 72 to 104, but is usually in the neighborhood of 80. Examination shows the movement to be good on both sides, only a little limited on the left. The note is a little hyperresonant over the whole left side, but nowhere tympanitic. Breath sounds are still almost completely absent. Fremitus is felt, but diminished in intensity. The whispered voice sounds are very distant with a suggestion of metallic quality. The roentgenogram shows the pneumothorax has largely cleared up, although the lower lobe is not yet completely expanded.

February 4. Patient feels well. He has at times fleeting pains about the chest. The heart is now in its normal position and the signs of the pneumothorax have entirely disappeared. All over the left front and over the upper left back numerous fine superficial scratchy rales are heard on deep inspiration.

February 18. Patient is feeling exceptionally well and is anxious to return to work. The physical signs show, as they have on all previous examinations, a little impairment and harsh breathing over the right upper lobe. The cutaneous and conjunctival tuberculin tests repeated on January 30 showed absolutely no reaction.

November 21. Patient was well until one week ago, when he began to have pain over the right front of the chest. Pain came on after slipping and straining his chest. Since then the pain has persisted, and he comes thinking a pneumothorax has developed again. He has a little cough and the pain is aggravated on coughing. He has taken his temperature the last few days, and it has constantly been a little over 99°. Patient looks well, his color is good, and he is in good spirits. Examination shows no evidence of pneumothorax. The percussion note is a little impaired above and below the right clavicle and in the supraspinous fossa where breath sounds are harsh and shrill. Over both the lower front and back there are a few coarse moist and a few fine crackling rales.

March 29, 1913. Patient comes complaining that for the past three or four days he has had severe pain in the lower left chest. The pain is particularly severe when he lies down. Last night he was unable to sleep on account of it. He thinks he has had a recurrence of the pneumothorax.

Examination. The patient looks well; is a little blue, probably from the cold. Percussion note is everywhere resonant, except for slight impairment over the right upper lobe. The heart is in its normal position. The lower borders of both lungs move freely on inspiration. Over the left lower front there is a shower of fine moist rales on deep inspiration.

August 2. About ten days ago patient was suddenly taken with severe pain in right side of chest. The following day on stooping over the pain was so severe that he fainted. His family physician told him the pain was due to pleurisy, and says he found tubercle bacilli in the sputum.

Examination. The patient's general appearance is as it has always been, quite good. Besides the impairment which has been heretofore noted on the right side, there are numerous moist and a few sonorous and sibilant rales over the whole front and in the supraspinous fossa in back. The sputum contains numerous tubercle bacilli. Patient admitted to the State Sanatorium.

April 25, 1914. Patient was at the State Sanatorium from August 27, 1913, to April 12, 1914. He has improved somewhat in his general condition, and has less cough and expectoration. The physical examination now shows impairment on the right to the third rib and fifth dorsal spine with harsh, blowing breath sounds and fine moist rales over whole front and to the sixth dorsal spine in back. On the left there is a little impairment above and below the clavicle, and in the back down to the third dorsal spine

with roughened breath sounds and moist rales above and below the clavicle and in the supraspinous fossa.

While the case above detailed was under observation I had the opportunity of seeing another instance of pneumothorax coming on in a healthy young man without apparent cause which ran an almost symptomless course and subsided completely in a few weeks:

CASE II.—*Healthy young man has sudden pain in left side of chest followed by dyspnea on exertion; examination the following morning, November* 30, 1910, *reveals complete left pneumothorax; uneventful recovery in four weeks; has remained well since.*

White male, aged twenty-nine years, came to me for examination on November 30, 1910. There was nothing of importance in the family history. He had always been strong and healthy, except that since childhood he had had attacks of renal colic often associated with hematuria. Detailed examination had shown a large left hydronephrosis with almost complete absence of renal function on that side. On the evening of November 29, as he was leaving his house after dinner, he suddenly felt a sharp pain in the left side, followed by a sensation as though something had given way. He went to his office and again experienced the pain, especially on movement. He felt as though inspiration did not fill out the left lung; as he expressed it, "as though air went only half-way down the chest." However, he did not feel ill and had no shortness of breath. He attended a meeting of the Bar Association, after the meeting enjoyed a light collation, and then walked with a friend to his club, about two miles away, and sat there reading until midnight. On the morning of November 30, as he left home, he again experienced the curious sensation in the left side. He had an appointment on that morning to have Roentgen-ray pictures taken of his kidneys; he reported to Dr. Geraghty for this purpose, who postponed the investigation when he heard of the patient's symptoms, and sent him to me for examination.

Patient was a large, well-nourished man of good color and healthy appearance. Chest well formed and symmetrical. Inspection revealed at once a marked difference in movement on the two sides of the chest, the right moving freely, the left very little. Percussion note was resonant over both sides—a little hyperresonant over the left, though the difference between the two sides was not marked. The breath sounds were absent over the left side. On the right the lower border of the lung was at the eighth rib in the axillary line and the lower border moved 8 cm. on deep inspiration; on the left the lower border of resonance was at the tenth rib and did not move on deep inspiration. The point of maximum impulse was not definitely visible. There was very little cardiac dulness to the left of the sternum. The heart sounds were much louder on the right than on the left. Roentgen-ray examination showed a well-marked pneumothorax on the left side. The upper

lobe markedly collapsed; the lower lobe widely separated from the diaphragm, but adherent to the chest wall in the axillary area at about the fifth rib. The heart moderately displaced toward the right.

December 19. Patient spent a week in bed and then began going about. He has had absolutely no fever, and the pulse and respiration rate have been normal. He has felt perfectly well except for a feeling of uneasiness in the left side when he bends over.

Examination. There is still considerable diminution of movement on the left side. Fremitus is well felt on the left but not nearly so well as on the right side; the breath sounds are heard on deep inspiration, and are then vesicular in quality. Over the lower front and below the angle of the scapula behind there are numerous fine moist crackling rales on deep inspiration.

January 1. Roentgen-ray examination shows that the pneumothorax has completely cleared up. The mediastinal shadows are dense and broad shadows radiate from the mediastinum toward the periphery. The shadows are denser in the right upper lobe than elsewhere. The heart is in its normal position.

January 7. Patient feels quite well; he has taken his temperature continuously and has had no fever. Occasionally he has a stitch in the left side.

Examination. Movement is almost equal on the two sides, perhaps a little diminished on the left. The left clavicle is a little more prominent than the right. Percussion note is everywhere resonant and the breath sounds are loud and vesicular on the two sides. At the left base there are a few fine rales on deep inspiration. The *A. r. z.*—right, 6 cm.; left, 7 cm. The 1 per cent. conjunctival tuberculin test is negative; the cutaneous test gives a slight reaction.

January 1, 1915. Patient has been seen frequently since his recovery from the pneumothorax. He has remained well, has had absolutely no pulmonary symptoms, and the examination remains unchanged.

During the past year I have seen three more cases in many respects similar to the two described. Two of these are almost identical with Case II, while the other presents interesting points of difference.

Case III.—Dispensary No. F. 9082.

Healthy patrolman, aged thirty-eight years, has sudden pain on left side, followed by dyspnea on exertion; examination reveals left pneumothorax; uneventful recovery in four weeks; has remained well.

White male, aged thirty-eight years, came to the Johns Hopkins Hospital Dispensary July 7, 1913, complaining of severe pain in the left side. The family history contains nothing of importance. The patient has always been a healthy man, and has had no serious illness since childhood. He is a patrolman and works at night. On the morning of July 4, patient reached home early in the morning

and went to bed. About noon, when he arose, he had severe pain in the left side of chest. However, in the evening he went to work as usual, but noticed on making his rounds that he was rather short of breath. Since then whenever he lies down or walks he has noticed the shortness of breath. During this time he has had pain in the left side.

Examination. Patient is a large, well-nourished man of healthy appearance. Mucous membranes are good color; no general glandular enlargement. Teeth are in bad condition and there is well-marked pyorrhea. Chest is well formed, though for a man of his build is rather long and narrow. The shoulders droop considerably, the left a little more than the right. The costal angle is about 80 degrees. The clavicles are equally prominent. Movement is markedly restricted throughout the left side. Percussion note over the right lung is normally resonant and the breath sounds are everywhere vesicular. There are a few fine moist rales over the lower front and in the lower axillary area. The lower border of the right lung is at the eighth rib in the axillary line and moves 6 cm. on deep inspiration. In the back the lower border of the lung is at the eleventh dorsal spine, and there is an excursion of 6 cm. between deep inspiration and full expiration. Over the whole left side of the chest the note is hyperresonant and rather drum-like in quality. The lower border of resonance is at the ninth rib in the axillary line. This point does not change with respiration. In the back the lower border of resonance is at a point between the twelfth dorsal and first lumbar spine and does not move with respiration. Fremitus is absent over the whole left side. Above the clavicle the breath sounds have a distant amphoric quality; elsewhere they are inaudible. The whispered voice sounds are scarcely audible over the upper portion of the chest, while in the axillary area and below the angle of the scapula they have a distinct, ringing, metallic quality. Cardiac pulsation is seen to the right and left of the sternum; cardiac dulness extends 5.5 cm. to the left and 6.5 cm. to the right of the median line. Heart sounds are clear, much louder on the right than on the left of the sternum. The pulse is slow, 76 to the minute, good size, regular. The vessel wall is palpable. Abdomen is normal in appearance; no rigidity; no tenderness. The liver is not felt; area of liver dulness is not enlarged. Spleen is not felt; area of splenic dulness is not enlarged.

July 19. Patient feels well. When lying down or walking he often has a sensation of rubbing over the left lower front. He walks about now with little discomfort. The percussion note is less hyperresonant on the left than it was at the first examination, and the breath sounds are audible over the left upper front. Cardiac dulness extends 8.5 cm. to the left and 4.2 cm. to the right of the median line.

August 2. Patient feels fairly well. He still has a little pain

in the chest, and at times he has shortness of breath when he walks rapidly. The percussion note is now almost equal on the two sides. Fremitus is still somewhat diminished in intensity on the left, but it is well felt everywhere. Breath sounds are audible over the left side, not so loud as on the right, and are accompanied by a profuse shower of fine moist rales over the lower front. Cardiac dulness extends 9 cm. to the left and 3.5 cm. to the right of the median line. There is a distant pleuropericardial friction rub to the left of the ensiform.

September 1, 1914. Patient has not returned for examination, but in reply to a letter states that he has remained perfectly well.

CASE IV.— *Young man, aged thirty-five years with relatively inactive chronic pulmonary tuberculosis, suddenly has severe pain in the left side. Examination reveals left pneumothorax. No constitutional symptoms develop and the pneumothorax heals uneventfully in five weeks.*

White male, aged thirty-five years, came for examination on October 1, 1912. There is a marked history of tuberculosis in the family. Patient has always been well but never robust, subject to frequent colds, some continuing rather obstinately. During the previous spring he had had grip, and his physician found evidence of tuberculous trouble in the chest.

Examination. Patient is a sparely nourished man of good color but looks below par in health. Pupils are equal and react actively to light; eye movements are all normal; no general glandular enlargement. Chest is long and thin, the right clavicle a little more prominent than the left, right shoulder sags a little and a little curvature of the spine to the right in the upper dorsal region; diminution of movement over the right upper. On the right the note is impaired above and below the clavicle and in the supraspinous fossa; breath sounds are a little blowing in quality, and after coughing there is a small number of fine moist rales to the third rib in front and to the fourth dorsal spine in back. On the left the percussion note in impaired to the second rib and in the supraspinous fossa; breath sounds are harsh and a little blowing; a medium number of fine moist rales to the second rib in front and to the fourth dorsal spine in back. Opposite the second and third dorsal spine the whispered voice sounds have a bronchial quality. Area of cardiac dulness is not enlarged; heart sounds are clear. Abdominal examination shows nothing noteworthy.

January 5, 1914. Patient has been well except for occasional attacks of abdominal pain which were diagnosed appendicitis and in July, 1913, the appendix was removed. Since the operation patient has been very well and has gained somewhat in weight. He never has cough and has not had any expectoration. Yesterday afternoon, after dinner, he had a sudden, sharp pain in the left lower axillary region associated with a feeling as though he wanted

to take a deep breath. He went home without any distress, but feeling chilled got into bed. After a few hours he felt perfectly well except that on deep breathing and movement there was some pain on the left side. During the night patient had some pain over the whole left side, radiating to the left shoulder.

Examination. Patient is lying comfortably in bed. He says he feels perfectly well, except there is a little pain in the left side when he turns over. Patient looks well and is in good spirits. Temperature 98.2°; pulse 78; respirations 18. The chest is symmetrical. The movement is markedly restricted on the left side. The percussion note at once attracts attention, being markedly hyperresonant throughout the left side. The lower border of resonance in the anterior axillary line is at the ninth rib; in the back at the twelfth dorsal spine, and these points do not move on deep inspiration. Fremitus is felt all over the left side, but is markedly diminished in intensity. Above and below the clavicle and in the supraspinous fossa breath sounds are plainly audible, distant, and blowing in quality. Over a small area in the second and third interspace in the anterior axillary line there is frank and loud tubular breathing; elsewhere over the chest breath sounds are inaudible. The whispered voice sounds are diminished in intensity everywhere over the side without change in quality. Over the small area in the second and third interspace where the breathing is tubular there is frank bronchophony. On the right percussion note is resonant except there is a little impairment above and below the clavicle and in the supraspinous fossa. The breath sounds are loud and vesicular in quality. After coughing there are moist rales to the second rib and to the fourth dorsal spine. The lower border of pulmonary resonance is at the seventh rib in the anterior axillary line, in back at the eleventh dorsal space; the border moves freely with respiration. Cardiac pulsation is seen to the right and to the left of the sternum. Cardiac dulness extends 5 cm. to the left and 6 cm. to the right of the median line. Heart sounds are louder to the right than to the left of the sternum.

January 20. After spending a few days in bed the patient got up and has been going about. During this time he has had absolutely no fever and the pulse and respiratory rate have been normal. He has a little shortness of breath on exertion and some dull pain over the left side. The percussion note over the left front has completely lost its hyperresonant quality, but hyperresonance persists over the left back below the angle of the scapula. Fremitus is still much diminished in intensity. Breath sounds are now audible over the upper front and the whispered voice sounds are better heard. The lower border of pulmonary resonance is at the eighth rib in the axillary line and there is an excursion of 4 cm. on deep inspiration. Heart dulness extends 10 cm. to the left and 4 cm. to the right of the median line.

February 21. Patient now feels perfectly well except that at times he has a little twinge of pain on the left side. Examination shows that the pneumothorax has completely disappeared and the conditions are the same as they were on examination before the onset of the pneumothorax. On the right the note is impaired to the second rib and to the third dorsal spine and there are rales after coughing to the second rib and to the fourth dorsal spine. On the left the note is impaired to the second rib and to the fourth dorsal spine, and moist rales are heard after coughing to the third rib and in back down to the angle of the scapula.

December 12. Patient has been quite well; he has gained a little in weight; he never has cough or sputum; indeed, feels that he is in very good health and the pulmonary examination shows the same conditions as on February 21.

CASE V.—*A healthy man, aged twenty-nine years, suddenly has severe pain in the right side on the morning of July* 29, 1914, *followed by a little dyspnea on exertion. Examination on August* 17, 1914, *reveals a right-sided pneumothorax which has almost completely cleared up. Patient has remained well since then.*

H. T., white male, aged twenty-nine years, came for examination on August 17, 1914. There is nothing of importance in the family history. The patient, though never robust, has always been healthy. Whooping cough, measles, and scarlet fever in childhood; no serious illness since. On the morning of July 29, the patient took an early train and went into the diner and ordered breakfast. He was feeling in his usual good health. While sitting at the table he suddenly had a catch in his right side, which bent him over and immediately after he had a feeling of oppression and some difficulty in getting his breath. The pain in the side was increased whenever he took a deep breath. Following this the patient had a little cough and a little expectoration. The sputum has been examined a number of times and tubercle bacilli have not been found. His temperature has been taken frequently and occasionally has been a little above normal. The pain in the right side has almost completely disappeared although he still complains of a little soreness. During the past week he has had no shortness of breath on ordinary exertion.

Examination. Temperature, 98°; pulse, 80; respirations, 20; weight 114½ pounds; height, 5 feet 9 inches. Patient is a sparely nourished man. His complexion is a little sallow; mucous membranes are good color. Pupils are equal and react actively to light. Eye movements are all perfectly normal. Teeth are in good condition, there is considerable dentistry; no pyorrhea. The throat is a little injected; there is no gross abnormality. Posterior cervical glands are all easily palpable but not markedly enlarged; the glands below the angle of the jaw on both sides are a little enlarged; the epitrochlear glands are just felt; the axillary glands are easily felt.

The chest is long and rather thin; the costal angle is about 80 degrees; the right shoulder is considerably lower than the left and the right clavicle a little more prominent. Movement is diminished over the right side. The spine is straight. Percussion note over the right front is a little hyperresonant in quality. On the left it is normally resonant, the difference between the two sides being by no means marked. The lower border of resonance is at the ninth rib on the right side; at the eighth rib on the left in the midaxillary line. On the left side the lower border of resonance shows a movement of 5 cm. on deep inspiration, whereas on the right there is none, or at most not more than 1 cm. of movement. Fremitus is well felt over the right side, but it is diminished as compared with the left. On quiet breathing breath sounds are entirely absent over the right side; on deep breathing they are very faint and distantly tubular in quality. The whispered voice sounds are diminished in intensity, but have a distant bronchial quality, and just below the calvicle they have a slight metallic quality. On the left breathing is everywhere loud and vesicular; no rales are heard. Heart: The point of maximum impulse is in the sixth interspace just inside the nipple line. Cardiac dulness extends 11 cm. to the left of the median line; there is no cardiac dulness to the right. The heart sounds are perfectly clear. They are absent to the right of the sternum. Abdomen is normal in appearance; abdominal wall is soft and relaxed. Liver is not felt; liver dulness does not extend below the costal margin. Spleen is not felt; area of splenic dulness is not enlarged. The right kidney is just palpable; the left is not felt. Pulse is regular, good volume and good size; the vessel wall is not thickened. Blood-pressure: systolic, 120; diastolic, 70. Roentgen-ray examination shows pneumothorax of the right side. However, the lung has expanded so that at some points it has almost reached the chest wall. Marked increased density of the mediastinal shadows and of the shadows generally throughout the lung. There is slight clouding and flattening of the left apex.

November 1, 1914. The patient has not been seen again, but reports that he has remained perfectly well.

Discussion. These five cases are of interest, since they illustrate (1) how insidious may be the onset of pneumothorax; (2) what few symptoms it may occasion; (3) how easily upon a casual examination the condition may be overlooked; (4) the perfectly benign course of the affection; (5) the occurrence of an insidious benign type of pneumothorax in perfectly healthy individuals as well as in those with manifest pulmonary disease.

This benign type of pneumothorax coming on without apparent cause and subsiding uneventfully has received a fair share of literary attention. The condition has been frequently described in England, less commonly in France, only occasionally in Germany, and though there are a few good accounts of it in American literature,

still it has not attracted wide consideration. Fussell and Riesman[15] reviewed the literature of spontaneous pneumothorax in 1902 and analyzed 56 cases. Nikolsky,[29] in 1912, collected 90 cases from the literature. Some authors emphasizing the obscure cause of the pleural rupture have termed the condition "spontaneous pneumothorax" (Nikolsky,[29] Emerson,[11] Bach,[3] Hamilton[20]); "idiopathic pneumothorax" (Boland,[7] Francine and Landis[14]), and "pneumothorax in the apparently healthy" (Weber,[37] Hall,[19] Male[27]), to distinguish it from pneumothorax following violence or gross pulmonary disease. Others, struck by the absence of the usual symptoms accompanying pneumothorax, have described it as "latent pneumothorax" (Bevan,[5] Stevens[36]), "pneumothorax with insidious onset" (Pepper[30]). Still others, having missed certain classical physical signs of pneumothorax, have called it "pneumothorax muet" (Yaldizdjian[41]) and "pneumothorax silencieux" (Adler[2]). Finally, many have emphasized certain salient features, using such descriptive terms as "recurring pneumothorax" (Finny,[12] Gabb,[16] Sale[35]), "pneumothorax with rapid recovery" (Coghlan,[10] Beevor[4]), "spontaneous, non-tuberculous pneumothorax" (Fussel and Riesman[15]), "curious instance of pneumothorax" (Jochmann[22]), etc.

None of the terms that have been suggested for this type of pneumothorax are satisfactory, but "spontaneous pneumothorax" is the term most commonly employed; and though it describes only one of the many important features of the condition, still it is the least objectionable, if we will accept its extension to embrace them all. In this sense spontaneous pneumothorax signifies a pneumothorax coming on in apparently healthy individuals without ascribable cause; resulting in no infection of the pleura and therefore unaccompanied by constitutional symptoms; and healing rapidly and completely in a few weeks.

As regards the meaning of "apparently healthy," I may say that most authors would exclude from the group of spontaneous pneumothorax those cases in which examination before or after the occurrence reveals definite pulmonary disease. The "non-tuberculous" nature of the condition is constantly emphasized. I feel very strongly that no such sharp line can be drawn, and I would include tuberculous cases that meet the other requirements of the definition. Case I certainly belongs to the group of spontaneous pneumothorax, and still years later he developed a manifest pulmonary tuberculosis. Both immediately before and immediately after the attacks of pneumothorax the clinical evidence was not sufficient to make a diagnosis of pulmonary tuberculosis, although in the light of later developments it seems certain that even at that time he must have had the infection. Cases II, III, and V in no way distinguishable from Case I have remained well. Case IV, though in good general condition, still had a definite pulmonary

tuberculous lesion before the onset of the pneumothorax. In all other respects the clinical picture was identical with that of the three previous cases. The absence of grave pulmonary disease, of pleural infection, and of mechanical conditions leading to high intrapleural pressure distinguish the condition from pneumothorax as it usually occurs in pulmonary tuberculosis. Later I will speak of the mechanism of the production of the pneumothorax in spontaneous pneumothorax and here wish only to remark that in all probability the mechanism in Case IV was the same as in the previous cases, and was not due, as pneumothorax in advanced pulmonary tuberculosis usually is, to the rupture of the pleura by a tuberculous focus.

While most cases of spontaneous pneumothorax remain simple, in a small number pleural effusion develops. Cases in which the effusion is the expression of an infection must be discarded from the group, but in a certain number the fluid remains sterile, no constitutional symptoms develop, and the fluid and air are both rapidly absorbed. Such instances are reported by Francine and Landis,[14] Hamilton[20] and West.[38] In some instances the fluid is bloody, apparently due to hemorrhage at the time of the pleural rupture. Rolleston's case[34] proved fatal and no cause for the pneumothorax or hemorrhage could be found at autopsy. Pitt's patient,[31] a lad, aged eighteen years, died within thirty-six hours of the onset of pain in the side. At autopsy a ruptured emphysematous bulla was found with a torn adhesion attached near it. Boland's patient[7] recovered after aspiration of thirty-four and then thirty-nine ounces of blood. Ness and Allen's patient[28] recovered uneventfully; apparently the hemorrhage was very small.

As regards the third characteristic in the definition, rapid and complete healing, one can set no absolute limit. In most cases the pneumothorax disappears in from four to eight weeks. Occasionally the pneumothorax will persist longer than eight weeks and then clear up completely, but a duration of over eight weeks is against including the case in the group of spontaneous pneumothorax.

The changes in the lung that occasion the pleural rupture are not clinically ascertainable, but there are enough autopsies on record to make clear the mechanism in many instances. Zahn,[42] in 1891, published the first thorough study of "pleural rupture without inflammation," and described four different modes:

First, the rupture of vesicular blebs. In one case he reports there were a number of such bullæ in the region of the apex of the left lung, and upon inflating the lung one of these showed a small rent. In another instance associated with well-marked pulmonary emphysema, numerous bullæ were found on the surface of the right lung, some as large as a hen's egg; one of these showed a tear 2 mm. in length. Zahn collects from the literature similar observations by Duvilliers, Dittrich, Fraentzel, and Rheder. Rankin,[32]

and Cnopf[9] may be added to the list. Bach[3] collects fifteen cases from the literature.

Second, the rupture of interstitial emphysema blebs. In these cases air enters the interstitial tissue, then reaches the pleural surface, where a vesicle is formed, which then ruptures. All such instances of interstitial emphysema have been about pleural adhesions, and the pleural adhesions are the primary condition which give the mechanical explanation for the interstitial emphysema. Zahn[42] reports two instances of pneumothorax produced by this mechanism. In both instances there was associated pulmonary tuberculosis, but the pleural rupture was about adhesions and not contiguous to tuberculous foci. He considers this the most common cause of rupture in spontaneous pneumothorax.

Third, a direct tear of the pleura by the tug of adhesions. Zahn[42] reports such a case in a suicide, and thinks the instance reported by Robertson belongs to this group.

Fourth, senile atrophy of the pleura. A man, aged sixty-one years, with extreme emphysema, showed at autopsy a number of minute openings in the pleural surface over an area where the membrane was extremely thin. Zahn remarks that he had never before seen such an extreme grade of emphysema, and he regarded the pleural atrophy to be due to pressure. I have encountered no similar observation in the literature.

We may exclude division four, since it is an unusual cause of pneumothorax, and it is a technical refinement to separate divisions two and three. Such postmortem evidence as is available, therefore, points to the rupture of vesicular emphysematous blebs and the tears produced by adhesions as the two common causes of spontaneous pneumothorax. The not infrequent finding of ruptured vesicular blebs has led some authors, for instance Bach,[3] to speak of the whole group under consideration as "spontaneous pneumothorax in emphysema." Anyone who has had a large experience with pulmonary cases will remark at once how surprisingly infrequent pneumothorax is in the frankly emphysematous. It is noteworthy that spontaneous pneumothorax is a disease of early adult life, over 80 per cent. of the instances collected by Nikolsky occurring before the age of forty years. Therefore, it is manifestly improper to regard spontaneous pneumothorax as having any direct relation to general pulmonary emphysema. When emphysema is its cause the emphysema is generally a local condition, and clinical evidence is, in my opinion, strongly in favor of adhesions being the usual condition underlying the pleural rupture.

Having in mind the mechanism of spontaneous pneumothorax, it will appear unreasonable to exclude from the group cases with pulmonary tuberculosis in which the onset and benign course of the pneumothorax and the rapid recovery are the characteristic features (such cases are reported by Coghlan,[10] Knight,[23]

Hamilton[20]). There is considerable evidence to influence us to believe that tuberculosis is the commonest cause of pleural adhesions, and if this be true it is further reason against drawing too close a line between manifest and obscure pulmonary tuberculosis, a distinction that at once involves serious clinical difficulties. Of course, it is possible that an isolated tubercle situated upon the pleura might rupture and the opening be so small that it would heal promptly without the pleura becoming infected. Such an occurrence, however, must be very uncommon. Letulle reports a diabetic without evidence of pulmonary disease who developed pneumothorax. Eight days later he died suddenly and autopsy revealed a single tuberculous nodule in the lung which had ruptured. West[38] and Flint[13] report instances of pneumothorax due to the rupture of a single small tuberculous cavity. However, neither of the cases resembled clinically spontaneous pneumothorax, for West's patient died shortly after the onset of pneumothorax from exhaustion, and although Flint's patient died of pneumonia, the hydropneumothorax had persisted for a long time before.

The clinical symptoms in spontaneous pneumothorax indicate that in most instances the pleural opening is very small. Symptoms of high intrapleural pressure are seldom present, and in the two cases I followed carefully with Roentgen-ray examinations the lung was not fully collapsed. Apparently as soon as sufficient air escapes into the pleural cavity to cause an appreciable decrease in the intrapulmonary pressure the pleura is relaxed and the opening closes. The size of the opening will determine the degree of pulmonary collapse.

In the definition of spontaneous pneumothorax the salient clinical features were emphasized. Briefly, the important points are these: The condition predominates in males: 45 males to 10 females in Fussell and Riesman's[15] series and 73 males to 14 females in Nikolsky's[29] group. The vast majority of the cases occur in young adults. In Nikolsky's table two instances are under fifteen years of age, 34 between fifteen and twenty-five years, 26 between twenty-five and forty years, 11 over forty years. The right and left side are affected with equal frequency. The exciting cause in many instances is exertion, though the exertion may be slight and entirely out of proportion to the result. Not infrequently the pneumothorax comes on without any provoking cause, and in some of the reported instances it developed during sleep (Fussell and Riesman,[15] Landmann,[24], Heitler,[21] Sale,[35] Bevan[5]). Nikolsky's analysis shows that an equal number follows exertion and comes on without exertion. The insidious onset is emphasized particularly by Pepper[30] and Jochmann.[22]

The symptoms at onset vary from extreme dyspnea and collapse to disturbances so slight as scarcely to attract attention. In the instances reported in this paper, pneumothorax would not be

suspected from the symptoms. Nearly always there is some dyspnea on exertion, but there is seldom distress when the patient is at rest. The mild character of the symptoms is a peculiar and characteristic feature of the condition. No doubt the size of the rupture largely determines the intensity of the symptoms. Cough is often present, but frequently is entirely absent, and is seldom troublesome. A characteristic feature of the condition is the absence of constitutional symptoms, of fever, and of other evidence of infection.

The duration of the pneumothorax varies. In most instances there is complete restitution in six weeks. Of 66 cases collected by Niklosky,[29] 59 recovered completely within two months; 6 during the third month; 3 during the fourth month. There are certain curious instances of pneumothorax that have persisted for a long time. Bittorf[6] reports a case which under his observation remained unaltered for a year and a half, and from the history he concluded that the pneumothorax had probably been present for twenty-five years. Whitney[39] thinks in his patient the pneumothorax had arisen seven years before his examination. Adams' patient recovered after the pneumothorax had persisted for five years.

I have found in the literature sixteen instances of recurrence of the pneumothorax (Jochmann,[22] Hall,[19] Bull,[8] Goodhart,[17] Gabb,[16] Sale,[35] Finney,[12] West,[38] Flint,[13] Knight,[23] Weber,[37] Rendu,[33] Maillart and Lasserre,[26] Wieruzski,[40] Grenier,[18] Bach[3]). Gabb's patient had four attacks all on the same side. Sale's patient apparently had eleven attacks during six years. In many of the cases the recurrence was, properly speaking, a relapse, the second attack of pneumothorax coming so promptly upon the resolution of the first as to warrant the inference that the original tear had reopened. Three of the cases are of particular interest, since, as in Case I of this report, the recurrence occurred on the opposite side. Goodhart's patient, a young man, aged twenty-four years, had a pneumothorax of insidious onset on the right side in May, 1891, another coming on in like manner in July, 1892, but on this occasion affecting the left side. He recovered from both attacks uneventfully, and was well three years, after. Wieruzski reports about a physician, aged fifty-four years, who had had bronchitis and emphysema for a long time. In the fall of 1894 he had pneumothorax on the right side that cleared up completely in about five weeks, but recurred a few weeks later. In February, 1899, he again developed pneumothorax, this attack being on the left side, which likewise cleared up in a few weeks. In September, 1899, he had another attack on the right side. Grenier gives the account of a young man, aged twenty-one years, who had a spontaneous pneumothorax on the left side in the fall of 1903. In December, 1904, he had an identical attack involving the right side, and in March, 1905, a

recurrence upon the right side. Recovery from all three attacks was rapid and uneventful.

After an attack of spontaneous pneumothorax the individual may remain well indefinitely. One of Hamilton's patients was well after ten years; another after six years; Fussell and Riesman's case after seven years; Bach's three years; West's ten years. A characteristic case of spontaneous pneumothorax was in the Johns Hopkins Hospital in January, 1898.* The patient returned to the hospital in November, 1913, complaining of digestive disturbances and jaundice. During the interval he had been well and had had no pulmonary symptoms. The pulmonary examination on the second admission showed no abnormality other than a few crackling rales at the left base.

As regards the examination it is important to emphasize that in these cases the physical signs of pneumothorax stand out in classical purity. Pneumothorax is so frequently accompanied by effusion and associated with gross disease of the lungs that there is a general tendency to emphasize accessory physical signs, namely, succussion, the coin sound, metallic tinkling, and movable flatness, rather than the fundamental signs peculiar to and characteristic of the condition. Laennec's description has been weakened by unessential additions. On inspection the affected side is not strikingly prominent, but there is always diminished mobility. Fremitus may be absent, but it is usually well felt, though greatly decreased as compared with the opposite side. The percussion note may be but little altered, and the change escape notice if the examination be hurried. On careful percussion the note is discovered to be hyperresonant, sometimes with tympanitic overtones. The striking feature on auscultation is the absence or great diminution in the intensity of the breath sounds. The voice sounds are less strikingly suppressed, and at times have a curious, characteristic metallic echo.

I wish to call attention particularly to the diagnostic value of percussion. Percussion of the lower lung border reveals that resonance stops on the affected side at the level reached by the lung on the sound side in full inspiration. This point is stationary, showing no variation with inspiration and expiration. The extension of pulmonary resonance to the full capacity of the pleural space with absence of respiratory variations at the border is absolutely characteristic of pneumothorax without effusion. If the note is hyperresonant the hyperresonance extends in front to the opposite border of the sternum. The heart is always displaced, and its position can be determined satisfactorily only by percussion.

The diagnosis is easily made if one thinks of pneumothorax, but in the entire absence of symptoms the condition may not be

* Reported by Osler, Maryland Med. Jour., 1898, xxxviii, 461; Case 28 in Emerson's report.

suspected and the physical signs be overlooked. Case I at first attracted attention as an instance of unusually feeble breath sounds, without any satisfactory explanation for the enfeeblement. A physician experienced in the study of pulmonary disease saw this patient, and was sure he would have missed the diagnosis had the condition not been pointed out. Case III was first seen by an experienced instructor in physical diagnosis, who diagnosed a mediastinal tumor pressing upon the bronchus.

The treatment for the condition is to do nothing. The pulmonary collapse closes the pleural opening, the air in the pleural cavity is gradually absorbed, and as the lung begins to reëxpand the pleural rupture is tightly healed. Occasionally the pneumothorax recurs shortly after the lung has completely expanded, no doubt due to incomplete healing of the pleural wound.

REFERENCES.

1. Adams. A Case of Pneumothorax, Boston Med. and Surg. Jour., 1886, cxv, 397.
2. Adler. Du pneumothorax silencieux, Thèse de Lyon, 1908.
3. Bach. Ueber das Vorkommen des spontanen Pneumothorax bei Emphysem, Beitr. z. Klin. d. Tuberk., 1910, xviii, 21.
4. Beevor. Pneumothorax; Rapid Recovery, Trans. Clin. Soc., London, 1903, xxxvi, 260.
5. Bevan. A Case of "Latent" Pneumothorax, Lancet, 1904, i, 1652.
6. Bittorf. Zur Kenntniss des chronischen Pneumothorax, Münch. med. Wchnschr., 1908, lv, 2274.
7. Boland. Idiopathic Pneumothorax, with Recovery after Aspiration, Boston, Med. and Surg. Jour., 1900, i, 321.
8. Bull. Cited by Nikolsky.
9. Cnopf. Cited by Fussell and Riesman.
10. Coghlan. Case of Pneumothorax; Rapid Recovery, Lancet, 1904, i, 1052.
11. Emerson. Pneumothorax: An Historical, Clinical, and Experimental Study, Johns Hopkins Hosp. Rep., 1903, xi, 1.
12. Finny. A Case of Recurrent Pneumothorax without Effusion, Ending in Recovery, Dublin Jour. Med. Sci., April 1, 1898, 273.
13. Flint. Practice of Medicine, 1873, 4th ed., 171.
14. Francine and Landis. A Case of Idiopathic Hydropneumothorax, with Complete Recovery, Med. Rec., 1909, lxxvi, 856.
15. Fussell and Riesman. Spontaneous Non-tuberculous Pneumothorax, Amer. Jour. Med. Sci., 1902, cxxiv, 218.
16. Gabb. Recurrent Pneumothorax, British Med. Jour., 1888, ii, 178.
17. Goodhart. A Case of Pneumothorax, First on the Right Side, a Year Later on the Left Side, and upon Both Occasions without any Discoverable Cause, Trans. Clin. Soc., London, 1896, xxix, 109.
18. Grenier. Le "Pneumothorax des conscrits" observe trois fois (une fois a gauche, puis deux fois a droite) chez le meme sujet, Bull. Med., 1905, xix, 987.
19. Hall. On Cases of Pneumothorax in Persons Apparently Healthy, Trans. Clin. Soc., London, 1887, xx, 153.
20. Hamilton. Some Further Observations in Pneumothorax with Especial Reference to "Spontaneous Pneumothorax" or Pneumothorax in those Apparently Healthy, Montreal Med. Jour., 1908, xxxvii, 492.
21. Heitler. Cited by Weber.
22. Jochmann. Ein eigenartiger Fall von Pneumothorax, Ztschr. f. klin. Med., 1902, xlv, 97.
23. Knight. Cases from Dr. Church's Wards, Case IV, St. Bartholomew's Hosp. Rep., 1890, xxvi, 294.
24. Landmann. Cited by Weber.

25. Letulle. Cited by Weber.
26. Maillart and Lasserre. Cited by Emerson.
27. Male. Pneumothorax in the Apparently Healthy, British Med. Jour., 1910, i, 1110.
28. Ness and Allen. Hemopneumothorax without Traumatism, British Med. Jour., 1910, i, 744.
29. Nikolsky. Ueber den spontanen Pneumothorax, Inaugural dissertation, Giessen, 1912.
30. Pepper. The Insidious Onset of Pneumothorax, AMER. JOUR. MED. SCI., 1911, cxlii, 522.
31. Pitt. A Case of Rapidly Fatal Hemopneumothorax Apparently Due to Rupture of an Emphysematous Bursa, Trans. Clin. Soc., London, 1900, xxxiii, 95.
32. Rankin. Cited by Fussell and Riesman.
33. Rendu. Cited by Emerson.
34. Rolleston. A Case of Fatal Hemopneumothorax of Unexplained Origin, Trans. Clin. Soc., London, 1900, xxxiii, 90.
35. Sale. A Case of Recurrent Pneumothorax, Lancet, 1907, i, 1572.
36. Stevens. Latent Pneumothorax, Lancet, 1905, i, 1124.
37. Weber. The Clinical Forms of Pneumothorax, Especially Pneumothorax in Pulmonary Tuberculosis and Pneumothorax Arising in Apparently Healthy Persons, Ztschr. f. Tuberk., 1903, iv, 477.
38. West. The Prognosis of Pneumothorax with Some Statistics as to Mortality and Duration and an Account of a Series of Cases of "Recovery," Lancet, 1897, i, 1264.
39. Whitney. Some Practical Considerations Concerning Pneumothorax. Based on a Brief Report of Cases, Philadelphia Med. and Surg. Jour., 1886, cvx, 397.
40. Wieruzski. Second Attack of Simple Pneumothorax in an Emphysematous Patient, Vratsch, 1900, xxi, 1516.
41. Yaldizdjian. Les Pneumothorax muets, Thèse de Paris, 1908.
42. Zahn. Ueber die Entstehungweise von Pneumothorax durch continuitatstrennung der Lungenpleura ohne eitrige Entzundung, Virchows Archiv, 1891, cxxii, 197.

THE OCCURRENCE OF ARTERITIS IN MENINGITIS.

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THE part played by inflammation in alterations of the intima of arteries is still an unsettled question. This is illustrated by the wide diversity of opinion which prevails among many of the foremost investigators. Some (Adami, Thoma, Jores) are of the opinion that the cases of chronic thickening of the intima are usually dependent upon mechanical disturbances, while others (Klotz, Hansen, Simnitsky) have shown that similar intimal changes may be found in the arteries of young individuals who had suffered from acute infectious diseases. The adherents of the mechanical theory hold that the intimal thickenings are commonly secondary to a medial weakening.

Rokitansky, an early investigator of nodular thickenings of the intima, held that they were the result of an organization of materials deposited from the blood stream upon the intimal surface of the

vessel. He was of the opinion that the intima, being a non-vascular structure, was not capable of undergoing an inflammatory change. The error of this view was clearly shown by Virchow, who described "endarteritis chronic deformans" as a parenchymatous inflammation of the intima, with active proliferation of the cellular elements and at the same time a metamorphosis of the intercellular substance.

Klotz has pointed out that the nodular aorta is the result of repeated insults telling upon the intima alone, and that the thickenings may be entirely proliferative, representing a chronic inflammatory production. Concerning the nodular thickenings about the intercostal arteries, he finds the reaction an inflammatory one and accompanied by progressive as well as degenerative changes in the tissues of the intima.

Again, we find that an endarteritis has been induced experimentally by the employment of various microörganisms. Klotz, who injected rabbits intravenously with B. typhi and streptococci of low virulence, obtained warty thickenings of the first part of the pulmonary and ascending limb of the aorta. Microscopically, these areas showed a fatty degeneration of the subendothelial tissue, with much connective tissue advancing into the degenerated area. Saltykow has noted similar results by the intravenous injection of staphylococci.

Boinet and Romary by the employment of different organisms (B. typhi, B. coli, streptococci, staphylococci, B. anthrax, tubercle bacillus, tetanus, and diphtheria) observed that tiny yellow plaques were produced in the aorta. Microscopically, there was a cellular infiltration in the intima, at times extending into the remaining layers, but most frequently almost entirely isolated to the adventitia around the vasa vasorum. Pernice studied the effect of the Staphylococcus aureus and found an inflammatory reaction in all three coats, consisting mostly of a round-celled infiltration, and in the most severe cases the inner layers of the intima contained large cellular elements.

Sumikawa, who irritated the vessels by painting them with turpentine or silver nitrate or again infected them with bacteria, demonstrated that the vessels so treated showed an inflammatory reaction in all the coats or else in the intima alone. It has been shown by Stumpf that in cases of infection by direct continuity the process proceeds from the adventitia inward and may advance to the intima, which may in turn develop a verrucose endarteritis.

Thus we find that not only is there a true endarteritic thickening of inflammatory origin, but also that the intima is capable of showing a definite inflammatory reaction with the presence of a cellular infiltration. However, the mode by which this reaction takes place, the relation of this inflammation to the different structures within the coats, is still open to discussion.

Koester believed that the primary lesion of arteriosclerosis was

an inflammation of the media. There is, he said, a chronic inflammation following the vasa vasorum from the adventitia into the media while the intimal reaction is only secondary to this. He further found that each plaque of endarteritis had one or more complementary areas of mesarteritis beneath it. In regard to the above discussion by Koester, we find the following noted in the recent work of Klotz. "The simultaneous presence of a small-celled infiltration in the vicinity of the vasa vasorum and the intima may be observed during the acute stages, but we have not been able to demonstrate a constant relation between them in the arterial wall. The localization of one or other in the artery is not always accompanied by a similar reaction in the other arterial coat opposite to it. In other words, though an inflammatory reaction may be demonstrated about the vasa vasorum in the adventitia and outer portion of the media a similar process may not be opposite to this in the intima. Moreover, where the simultaneous presence of a cellular infiltration has been observed in the inner and outer coats of the artery there has always appeared a strip of media adjacent to the intima which was uninvolved in the inflammatory process. It would, therefore, appear that these reactions are individual, though frequently occurring side-by-side in the same vessel. The cellular exudate found in the intima appears to arise by a direct migration of the wandering cells from the surface of the artery."

Although inflammatory diseases of the intima have long been recognized, we, nevertheless, feel that the exact character of the lesion is not generally recognized. It was not until recently that there has been specific information concerning this subject, and we would like very much to add supporting evidence to a process already so accurately described by Klotz.

In a previous study upon the reactions of elastic tissue to inflammation we have briefly made mention of the reaction seen in the vessel walls in a case of acute septic meningitis. Following this work we thought it of special interest to study the changes in the arteries of the meninges in the various types of acute meningitis. For this purpose we have selected cases of acute septic, tuberculous, syphilitic, and anthrax meningitis, together with blastomycosis of the meninges and acute anterior poliomyelitis.

The stage of the disease at which the patients died of acute septic meningitis always gave evidence of a simultaneous involvement of the meningeal arteries. At the beginning the intima was found very edematous and the cells widely separated, with a considerable pinkish staining granular debris between them. Whether this can be accurately taken as the initial stage in all cases is difficult to say. However, shortly following upon this edema there was seen a migration of inflammatory cells from the lumen of the vessel into the intimal tissues. Quite often inflammatory cells could be seen passing between the cells of the intimal endothelium, and it appeared as

though the endothelial cells were indented or plastic at these points of entrace. The endothelial covering of the intima could be made out in the majority of places and consequently allowed accurate study of the process. With the migration of these cells into the intima the latter became much thicker and more swollen, so that it formed a prominent, puffy inner layer (Fig. 1.) The cells which took part in this reaction consisted for the most part of polynuclear leukocytes, which extended through the entire dépth of the intima to the internal elastic lamina. However, associated with the polynuclear leukocytes there were a fair number of lymphocytes and large phagocytic endothelial cells. In some specimens these endothelial cells appeared in great numbers, simulating not a little the grouping of endothelial cells in the more chronic lesions. Furthermore, amid the collections of endothelial cells were seen other cells like fibroblasts arising from the fixed cells of the intima and having elongated oval nuclei and swollen spindle-shaped bodies of clear

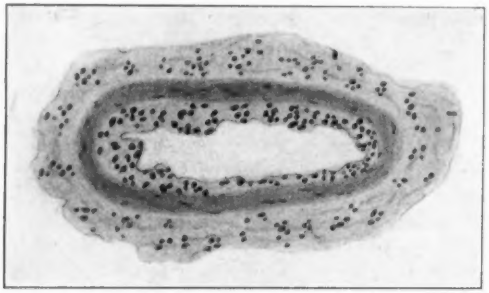

FIG. 1.—Septic meningitis. Acute inflammatory infiltration of intima.

cytoplasm. These cells appeared in the deep intima, but were also seen in the intermediate zone of this layer. The endothelial cells were large and round, with pale-staining protoplasm and centrally placed stippled nuclei. These cells were phagocytic for polynuclear leukocytes, lymphocytes, and a dark brown pigment.

In the intima of some of the vessels the pigment in the endothelial cells was not observed, while in others a fair amount of pigment, debris, and cells was found. The endothelial cells were often so crowded with phagocyted cells and material that it was difficult to make out the nucleus proper. In some instances a number of red-blood cells were also seen in the lesion of the intima. In most of the vessels studied the internal elastic lamina formed the outer boundary of the inflammatory infiltration of the intima. It would appear that the inner elastic membrane is a very resistant layer and limits the extent of the inflammation for a relatively long time, although ultimately the barrier is overcome.

The adventitia is commonly invaded by the exudate which covers the meninges. This exudate is made up of large numbers of polynuclear leukocytes with lymphocytes and a considerable number of endothelial phagocytes. These cells invade the adventitia, but curiously enough stop at the outer border of the media. The striking feature of this is that in the same artery the infiltration of the intima has stopped at the inner elastic membrane, so that the media is left intact. In vessels so affected the media at this time shows no deviation from the normal. It would be well to note that in these vessels there is no demonstrable relationship between the reaction in the adventitia and that in the intima, and hence that the media cannot be the site from which the extension into the intima occurs. Another noteworthy feature is that the adventitia is quite often comparatively free from inflammatory cells while the intima is densely infiltrated, the entire circumference being uniformly affected.

Although the media is uninvolved in the earlier stages, it, nevertheless, becomes involved later on. This takes place by the cells advancing along the lymphatics from the adventitia and to some extent from the intima. The extension from the intima takes place only in a very small part after the inner elastic membrane has been injured by the inflammatory reaction in the intima. The weakening of the elastic layer is demonstrated by a Weigert elastic stain, which shows splitting and granulation of the fibers with inflammatory cells lying between the elastic threads. The fine split threads of elastic tissue bend into the intima, and in many places they can be seen lying among the inflammatory cells close to the parent layer. Notching and granulation of the inner border of the elastic membrane was a very prominent feature in these sections.

When (Fig. 2) the inflammatory reaction involves the media it is more intense in the outer layers of this coat. From this appearance it would seem that the inflammatory reaction in the media comes for the most part by the extension from the adventitia and advances to the outer border of the inner elastic membrane but rarely goes further. When an inflammatory infiltration was observed in the media the invading cells were sparsely scattered and rarely included all of the types seen in the intima.

The intima of the arteries of the blastomycotic and anthrax meningitis showed extensive infiltration by inflammatory cells, polymorphonuclear leukocytes, together with a fair number of large swollen endothelial cells being the principal types of the exudate. The reaction in the intima was particularly acute. An occasional leukocyte with acid-staining granules was seen. Although the reaction was most marked in the intima, there were a considerable number of inflammatory cells in the media and adventitia. These cells were confined to the coat in which they were found, and the internal elastic lamina seemed to act as a limiting membrane.

We found it took a fair time for the inflammatory products to bring about a sufficient change of the elastic layer to permit diffuse cellular migration, in which the intimal and medial reactions commingle and appear as if they had been part of a single process advancing from without inward. The change noted in these vessels conformed to the more advanced reaction observed in the arteries of acute septic meningitis.

In the arteries of tuberculous meningitis the vessel wall was only mildly involved, compared to the types previously described. The intima was moderately swollen, with the presence of occasional lymphocytes and polymorphonuclear leukocytes. The involvement never reached the proportions seen in the more acute infections. Inflammatory cells were seen scattered in the muscular wall, but the reaction was more particularly perivascular in character. This periarterial inflammation with lymphocytes was also the type observed in the syphilitic meningitis and anterior poliomyelitis.

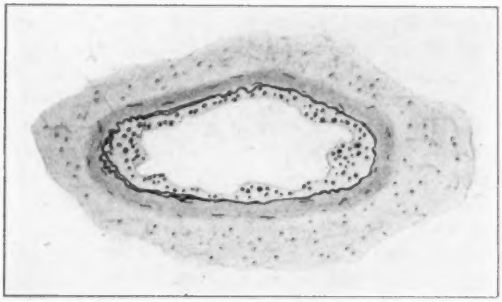

FIG. 2.—Septic meningitis. Splitting of elastic lamina through inflammatory process.

Sections of the acute septic meningitis stained with Sudan III, and hematoxylin showed the presence of fat in the cells contained within the intima. This fat was found in the form of fine granules, some of which were almost globular. It was present in the leukocytes and endothelial cells of the inflammatory infiltration. At times a slight fatty change was noted in the deep intimal tissue bordering on the elastic layer. The fat here appeared smooth and homogeneous. This was only slight in amount, and was not the rule, most of the fat being intracellular.

The presence of large endothelial cells in the intima of arteries have been described by Klotz and Anitschkow. Anitschkow fed rabbits with cholesterin mixtures and demonstrated doubly refractile lipoid bodies within endothelial cells in the intima of their arteries. Klotz noted that "similar cells may be commonly demonstrated in human arteries where the fatty degeneration occurs in the superficial layers of the intima, and when such specimens are cut (frozen)

on the flat they are seen as compact aggregations in which the lipoid substance is almost entirely intracellular." As previously mentioned we found endothelial cells in the intima containing fatty granules and small globules as well as other endothelial cells containing phagocyted cells, fat, and blood pigment. We would draw particular attention to the phagocytic character of the endothelial cells observed in our specimens, and to note that it is not at all unlikely that the endothelial-like cells noted by other observers are of the same type.

It is almost impossible to definitely indicate the final results which occur in the arteries that we have examined, as these particular diseases are so uniformly fatal. However, there are several points to bear in mind which direct our attention toward the probable outcome of the arterial lesion. We have seen that the inflammatory process in the intima is accompanied by progressive as well as degenerative changes. Fibroblasts, several layers deep, were found proliferating in the swollen intima, and fatty substances were present in the superficial infiltrating cells and only rarely in the region of the internal elastic lamina. Most of the lipoid substances were intracellular, and much of it would, in all probability, have been removed by active metabolism in the stage of healing. In the end the fibroblastic proliferation would have brought about repair of the injured layer, leaving the intima thickened and hyalin in appearance.

Virchow demonstrated that the intima, like other non-vascular structures, may be the seat of inflammation, and that a proliferation of its own cells leads to the nodular masses on the surface. Moreover, the endarteritic thickenings of the aorta about the intercostal arteries have been recently proved by Klotz to be of inflammatory origin. He found the reaction an inflammatory one, accompanied by progressive as well as degenerative changes in the tissues of the intima and repair accomplished by a proliferation of the connective tissues of the inner layer of the intima. It was further noted by him that inflammatory reactions of the intima of longer duration are always accompanied by a connective-tissue disturbance of a proliferative kind, and from them there develop the intimal thickenings of the "hyalin" type.

There is still another process which must not be passed unnoticed. the great tendency for thrombosis in these vessels. With the marked involvement of the intima and at times disorganization of this layer we have a factor enhancing the coagulation of blood. Added to this the narrowing of the vessel lumen, slowing of the blood stream at irregular points, and an abnormal reaction of the inflamed tissue still further assists in producing thrombosis. In many of the vessels of acute septic infection there is total destruction of the intima, with early thrombosis. Fibrin and inflammatory cells are found in the deep intimal tissues and take a position between the

split fibers of the internal elastic lamina. The repair of such a process would eventually lead to obliteration of the arterial lumen. This alteration in the structure of the vessel has been variously indicated as "endarteritis obliterans" (Friedländer), "endarteritis productiva" (Orth), "thromboangiitis obliterans" (Buerger), and a type similar to the last described by Winiwarter.

In our discussion we wish to be clearly understood that our observations have been limited entirely to the study of acute cases. Further, although we have studied a variety of affections of the meninges, our opinion as to the ultimate outcome of the changes found is based for the most part upon the reactions occurring in the arteries of septic meningitis during the acute stage. The organisms associated with this affection are the most common factors in the production of acute purulent lesions in the body. They are commonly associated with septicemia, pyemia, and ordinary infections, to which we are all subject. Our findings are, therefore, very suggestive that if the opportunity is taken to study the systemic vessels in the various stages of infectious diseases, the inflammatory character of the endarteritic process as described by Klotz, could in many instances be determined.

CONCLUSIONS. The intima, although a non-vascular structure, is capable of suffering an acute inflammatory reaction.

This inflammatory infiltration occurs by the direct migration of the wandering cells from the lumen of the vessel.

An inflammatory reaction in the intima is not always accompanied by the presence of inflammatory cells in the remaining coats.

Furthermore, a simultaneous infiltration of the intima and adventitia by inflammatory cells may occur without any involvement of the media.

Accompanying the inflammatory reaction in the intima there are alterations in the elastica interna similar to those described in a previous paper.

Although we have had only the opportunity of observing early proliferative changes in the lesions studied, we, nevertheless, are of the opinion that ultimate repair is brought about by the continued proliferation of the fixed cells of the intima.

I am indebted to Dr. S. R. Haythorn for the specimens of nodular syphilitic meningitis.

BIBLIOGRAPHY.

Adami. AMER. JOUR. MED. SCI., 1909, cxxxviii, 485.
Anitschkow. Ziegler's Beiträge, 1913, lvi, 379.
Boinet and Romary. Arch. de méd. exper., 1897, p. 902.
Buerger. Jour. Med. Research, 1914, xxxi, 181.
Friedländer. Zentralbl. f. d. med. Wissensch., 1876, No. 4.
Hansen. Ref. Klotz, Jour. Med. Research, 1915, xxxi, 409.
Jores. Wesen und Entwickelung der Arteriosklerose (Wiesbaden, 1903).
Klotz. Brit. Med. Jour., 1906, p. 1767.
Klotz. Jour. Med. Research, 1915, xxxi, 409.

Klotz. Jour. Med. Research, 1915, xxxii, 27.
Koester. Berlin. klin. Wchnschr., 1875, No. 31.
McMeans. Jour. Med. Research, 1915 (in press).
Orth. Ref. Thorel, Lubarsch-Ostertag, 1906, xi, Abt. i, 958.
Pernice. Atti. della R. Acad. delle Scienze Med., Palermo, 1895.
Rokitansky. Handbuch der speciellen path. Anat., 1844, p. 524.
Saltykow. Ziegler's Beiträge, 1908, xliii, 147.
Simnitsky. Ztschr. f. Heilkunde, 1903, xxiv, 177.
Stumpf. Ziegler's Beiträge, 1913, lxi, 417.
Sumikawa. Ziegler's Beiträge, 1903, xxiii, 242.
Thoma. Graefe's Archiv f. Ophthalm., 1889, xxxv, 1.
Virchow. Virchows Archiv, 1879, lxxvii, 380.
Winiwarter. Arch. f. klin. Chir., 1879, xxiii.

THE ROENTGEN EXPERT WITNESS.

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Courts of law depend upon facts. The legal value of medical testimony usually depends upon the introduction of a physician's expert opinion of an actual or a hypothetical case. There are rarely any tangible facts such as the exhibition of signed papers, defective machinery, etc. We may say that, generally speaking, expert medical testimony is inferential and based upon a physician's interpretation of actual or hypothetical symptoms, both objective and subjective. His opinion may be influenced, though not dishonestly, by this point of view or his medical training, experience and environment. The greater portion of the law with which the physician comes in contact is based upon personal damage suits. The extent of the injury to the plaintiff and its influence upon his health during the balance of his life, or for a lesser period, is the question which the physician is called upon to answer. The presence of actual damage to the permanent bony framework of the human body is of pertinent importance. This importance may be argued, but it is needless to argue that testimony which assures the judge and jury of actual bony damage or anatomical normality is of inestimable value.

Heretofore it has been possible to array upon both sides of a case medical talent capable of affirming or denying the actuality of a bony defect where the fracture was not compounded. Either diabolically or innocently, testimony adaptable to the lawyer's conception of his client's position could be secured.

Difference of opinion is not so much a matter of honesty or dishonesty as of temperament, environment, original concept, inheritance, public opinion and possibly least, knowledge of the subject. Therefore any medical testimony which presents tangible facts, either negative or positive, to a legal hypothesis is a valuable advance.

The apparent farcical yet perfectly legitimate inconsistency of the usual medical testimony is rarely apparent in Roentgen evidence.

The Roentgen-ray enters the medicolegal field with brilliant tangible evidence impossible of refutation if properly interpreted and adequately identified. No longer is it necessary to depend upon the mental conception of the surgeon who has merely inspected a patient's extremity when the actual shadows of the bony parts can be exhibited in court. While there remains the arguable question as to the importance or the influence or result of a fracture in a bone, there is no longer the necessity of medical conjecture as to its presence or absence.

The apparent forcefulness of Roentgen negatives does not necessarily imply their unconditional admission in courts of law. There is such latitude in the interpretation of even bony shadows as to seriously interfere with the unlimited bantering of such delicate scientific exhibits before a judge and jury of average citizens.

Let us consider a parallel in scientific evidence. For instance, a tract of land with a disputed boundary line its before the court. At the suggestion of the defendant the court appoints a disinterested surveyor to measure and plat the disputed land. The surveyor proceeds and then presents his testimony in court based upon the measurements made with surveying instruments. These instruments are necessary for the surveyor to come to exact conclusions as to the lay of the land and its dimensions, but he does not show his instruments to the jury. Another instance, a pathologist is asked to examine a tissue, let us say, the discharge of a supposedly pregnant woman. He proceeds to section the tissue, stain and examine it with the microscope. His opinion is the result of the use of these several instruments. Does he actually exhibit the microscopical slides to the judge and jury? No. Yet we constantly notice the actual exhibition of Roentgen negatives to the jury and permit the handling of these scientific instruments by jurymen who are wholly incapable to the least conception of shadow values.

The interpretation of Roentgen shadows is a matter of experience and a knowledge of anatomy and tissue density. The widely disseminated knowledge of photographic reproductions as to sharpness and accuracy of focus is not paralleled by contemporary Roentgen knowledge.

It is not best at present to assume any arbitrary position as to the admission of Roentgen testimony without the actual roentgenograms. There is little doubt but that the use of the actual Roentgen plates as a basis for Roentgen testimony does fortify the roentgenologist's evidence.

The Conduct of the Roentgen Expert in Court. The Roentgen expert should limit his testimony to the facts which he believes his Roentgen evidence tends to prove. He should not

consider that his qualifications as a Roentgen expert permits him to exercise opinions which are distinctly matters of surgical judgment.

The Roentgen expert should qualify himself by submitting his experience of a number of years of actual Roentgen practice, based upon previous training under recognized authorities, he may recite his scholastic training in medicine and his affiliations with the usual medical societies, especially noting the organizations within his own specialty; his hospital appointments attest recognition of his standing within his own community. His literary pursuits may be meritorious but are more a valuation of his industrious proclivities rather than of his professional or expert ability.

It is well understood as a legal proposition that the credibility of Roentgen evidence depends upon the science, skill, experience and intelligence of the party taking the roentgenograms and testifying thereto.

The prejudice of trial attorneys toward clients frequently leads them to promote exaggerations in testimony. They may also plan to go beyond the facts of Roentgen evidence to establish extraordinary claims of disability. The Roentgen expert must be wary when the questioning is not sharply confined to the facts as he understands them from his Roentgen examination alone. Otherwise he may tend to subtract from the value of his Roentgen evidence by the undue comprehensiveness of his knowledge.

The Roentgen expert must maintain a neutral attitude and should not permit any prejudice or sympathy to influence his opinion. He must not consider his work infallible and the distortions and artifice which may appear in his exhibits must not be reflected in his testimony.

Roentgen evidence, properly interpreted and carefully presented to the court and jury, can wield such an incontrovertible influence that the roentgenologist must need maintain a calm, dignified, ethical attitude and appearance.

A CLINICAL STUDY OF CHRONIC DIARRHEA.[1]

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The relative frequency of various causes of diarrhea depends in large part upon the place in which cases are studied. Chronic

[1] Read at the Annual Meeting of the American Gastro-enterological Association, Baltimore, Md., May 10, 1915.

bacillary and amebic dysentery are relatively rare in New York and its environs, and chronic diarrhea is therefore a far more infrequent complaint than it is in some regions. We must also recognize that etiological statistics will vary with the observer on account of personal bias, and will depend upon the particular therapeutic field that he has cultivated which determines in part the type of case he sees. This series of 74 cases of chronic diarrhea which we have had the opportunity to study thoroughly in the office and laboratory is made up entirely of selected ambulant cases, selected in the sense that the condition of the patient justified thorough and repeated examination, and also because cancerous and luetic ulceration of the colon has been excluded from the series, as they rarely give rise to true diarrhea, but merely a discharge of blood and pus.

We are including under the term chronic diarrhea a constant or almost constant looseness of the bowels, a troublesome increase in the number of daily evacuations. In the accompanying table I have arranged what now seems to me the most satisfactory classification of the abnormal conditions that occasion chronic diarrhea. We must admit, however, that with improvements in our methods of study it may become necessary to recognize the importance of other conditions which are not included in this list. In this particular series some of the more unusual conditions did not occur.

TABLE I. ETIOLOGY OF CHRONIC DIARRHEA.

1. Achylia gastrica.
2. Colitis.
   (*a*) Catarrhal.
   (*b*) Ulcerative.
      Simple bacillary.
      Amebic.
      Luetic.
      Cancerous.
      Tubercular.
3. Colonic stasis.
4. Emotional excitability.
5. Glandular disease.
      Pancreas.
      Thyroid.
      Adrenal.

The achylia group.

We shall confine the term achylia gastrica to those cases in which the test meal shows no free acid and the total acidity is twenty or under. The test meal is small in amount and shows little

TABLE II.

Number.	Age.	Sex.	Duration of symptoms	Gastric analysis.		Colitis.	Colonic stasis.	Other data.
				Free acid.	Total acidity.			
1	27	F.	3 years	60	80	.....	Marked	Neurotic.
2	65	M.	16 years	0	12	Atrophic	.....	Chronic nephritis.
3	40	M.	5 years	50	74	Ulcerative	.....	Non-amebic; hemorrhagic.
4	33	F.	3 years	0	20	.....	.....	Pulmonary tuberculosis.
5	47	F.	4 years	0	16	.....	.....	Goitre; acute thyrotoxicosis.
6	76	M.	6 years	0	10	Atrophic	.....	
7	42	M.	6 mos.	25	40	.....	.....	Graves' disease.
8	46	F.	1 year	20	35	Catarrhal	Marked	Neurotic.
9	38	M.	5 years	55	80	Catarrhal	Marked	
10	16	F.	1 year	..	..	.....	Marked	Rectum filled; spastic.
11	42	F.	2 years	0	12	Acute	No	Acute colitis in attacks.
12	43	F.	2 years	0	10	Catarrhal	No	
13	32	F.	3 years	0	15	Catarrhal	No	No relief from appendectomy.
14	39	F.	2 years	60	85	Catarrhal	No	Neurotic.
15	36	F.	1 year	0	15	.....	Marked	
16	38	F.	3 years	0	11	.....	.....	Tubercular enteritis.
17	35	F.	16 years	30	55	Ulcerative	.....	Amebic dysentery.
18	48	F.	6 mos.	35	70	.....	.....	Addison's (incipient).
19	49	M.	3 mos.	0	12	Catarrhal		
20	68	F.	3 years	..	..	Ulcerative	.....	Non-amebic; hemorrhagic.
21	28	F.	5 years	..	..	.....	Marked	Spastic balls in rectum.
22	46	F.	10 years	65	80	.....	Marked	
23	45	F.	8 years	20	36	Catarrhal	.....	Chronic pancreatitis; stones.
24	33	F.	4 years	25	40	.....	.....	Emotional; diarrhea.
25	51	M.	1 year	35	65	.....	.....	Addison's (incipient).
26	30	M.	2 years	30	45	.....	Marked	
27	33	F.	6 years	0	15	.....	.....	Neurotic.
28	36	F.	8 years	40	60	.....	.....	Addison's (incipient).
29	29	M.	3 years	35	55	Ulcerative	.....	Non-amebic hemorrhagic.
30	35	F.	4 years	40	60	Catarrhal	Marked	Neurotic.
31	35	M.	6 years	32	45	Catarrhal	.....	Severe proctosigmoiditis.
32	29	F.	1 year	20	35	Catarrhal	Marked	
33	48	F.	2 years	34	50	Catarrhal		
34	28	F.	10 years	0	12	.....	.....	Neurotic.
35	30	F.	3 mos.	20	52	Catarrhal	Marked	Spastic feces in colon.
36	42	F.	6 years	0	12	.....	.....	Neurotic.
37	64	M.	10 years	0	15	Ulcerative	.....	Cured by ipecac in five days.
38	47	M.	2 years	30	65	Catarrhal	.....	Severe proctosigmoiditis.
39	68	F.	1 year	..	..	Catarrhal	.....	Severe proctosigmoiditis.
40	62	M.	4 years	0	12	.....	Marked	
41	37	F.	5 years	30	47	Catarrhal	Marked	Severely toxic.
42	55	F.	5 years	..	..	Catarrhal	Marked	
43	30	M.	16 years	20	40	Ulcerative		
44	38	F.	12 years	0	16	.....	.....	Graves' disease.
45	28	M.	6 mos.	..	..	Ulcerative	.....	Non-amebic; hemorrhagic.
46	44	M.	1 year	0	14	Catarrhal		
47	34	M.	6 mos.	40	60	Catarrhal		
48	31	M.	1 year	0	18	Catarrhal		
49	29	F.	4 years	20	41	.....	Marked	Neurotic.
50	37	M.	3 years	29	55	Catarrhal	Marked	
51	38	M.	6 mos.	0	12			
52	53	M.	5 years	0	10	Catarrhal	.....	Pulmonary tuberculosis.
53	55	M.	10 years	0	12	Catarrhal		
54	33	M.	12 years	0	13	Catarrhal		
55	35	F.	2 years	20	40	.....	.....	Pulmonary tuberculosis.
56	35	M.	12 years	..	..	Ulcerative	.....	Amebic.
57	62	M.	6 years	0	20	Atrophic	.....	Cholelithiasis.
58	29	F.	1 year	30	50	.....	No	Hyperthyroidism.
59	32	F.	2 years	15	30	Catarrhal	Moderate	
60	34	F.	6 mos.	20	35	Catarrhal	.....	Graves' disease.
61	52	M.	1 year	20	35	Ulcerative	.....	Hemorrhagic; non-amebic.
62	37	M.	1 year	40	60	Catarrhal	Marked	
63	55	F.	7 years	15	25	.....	.....	Hyperthyroidism.
64	62	M.	3 years	0	15			
65	37	F.	6 years	25	40	.....	.....	Graves' disease.
66	61	M.	18 mos.	15	27	.....	.....	Addison's disease.
67	..	M.	3 years	0	20	Ulcerative	.....	Amebic.
68	35	F.	6 mos.	15	35	.....	.....	Addison's disease.
69	21	F.	5 years	30	50	Catarrhal	Marked	Spastic type.
70	17	F.	2 years	25	40	.....	Marked	
71	39	M.	2 years	35	55	Ulcerative	.....	Non-amebic; hemorrhagic.
72	56	M.	8 years	0	9	Catarrhal		
73	47	F.	1 year	30	55	.....	.....	Hyperthyroidism.
74	52	M.	3 years	15	45	Catarrhal	Intermittent	

chymification. Only on two occasions have I seen achylia disappear and free acid appear at a later period.

Of the 74 cases of chronic diarrhea in this series, 22 (or 34 per cent.) showed achylia gastrica. Diarrhea is not necessarily an accompaniment of failure of gastric digestion, as is shown by the fact that it is rarely seen in malignant disease of the stomach or after gastro-enterostomy for pyloric stenosis: and out of a total of 79 cases of achylia seen in my office, only these 22 had loose bowels. These statistics correspond closely with those published by Stockton[2] in a series of 132 cases of achylia. I have never seen a chronic diarrhea which I believed was explained by hyperchlorhydria. In those with diarrhea we might suppose there was a failure of pancreatic digestion, but this is contrary to our observation. The opinion that the diarrhea is of nervous origin is entirely untenable in a majority of cases. It is possible that in the constipation attending hyperacidity and the diarrhea of achylia we have some fundamental but as yet undiscovered fact of physiology, but at the present time we are, I think, forced to the conclusion that achylia is rather a predisposing cause of diarrhea, and that there is usually a direct exciting cause.

In studying these 22 cases I have been impressed with the number of times that concomitant conditions could be held accountable for the looseness of the bowels. In 8 cases examination disclosed a definite catarrhal colitis, and excellent results were secured solely by the treatment of the colitis. In 2 cases examination disclosed an amebic ulcerative dysentery, and the diarrhea was cured by ipecac therapy. In 3 cases there was colitis, and many organisms of the flagellate group were found in the fresh dejecta and gastric contents. Local treatment of the stomach and colon by irrigation resulted in temporary cessation of the diarrhea and the temporary disappearance of the flagellates, but no permanent relief. In 2 cases we have seen achylia gastrica in elderly men with atrophic colitis. In 4 cases there were periodic outbreaks of acute serous colitis characterized by the passage of enormous quantities of practically odorless fluid rich in serum albumin. In 2 cases there was a definite pulmonary tuberculosis and a considerable suspicion, although not entirely proved, of tuberculous enteritis. From these observations I am led to the opinion that achylia renders the individual more liable to chemical, mechanical, and microbic injury, which gives rise either to irritation of the colon with undue stimulation of peristalsis or to acute attacks of inflammation or to chronic changes in the mucosa.

My experience with the treatment of diarrhea associated with achylia has led me to view with considerable question some of the accepted ideas on the subject. So far as diet is concerned, I think

[2] Amer. Jour. Med. Sci., 1909, cxxxviii, 157.

that ordinarily it has less affect than we have been led to believe. Foods which are ordinarily laxative, such as fruits and fats, may occasion or continue the bowel looseness more than in the normal individual. But, on the other hand, some patients do fully as well and many better on a diet in which there is an abundance of indigestible residue. The limitation of proteid food because gastric digestion is lacking gives no satisfactory clinical results. In the small group of cases where there are frequent outbreaks of acute colitis it is sometimes necessary to persist in a bland diet such as would be used in any subacute gastro-enteritis. Hydrochloric acid therapy has never proved of much temporary or any permanent value, although I have tried it repeatedly in different doses. I have never seen any good results with any form of enzyme therapy. Astringent medications have in the main given only temporary relief.

In a few instances I have seen remarkable results with massive doses of tannigen, 5 grains every hour day and night, for several days. These have all been in cases of profuse, watery diarrhea of long standing in which all other measures have failed. The more satisfactory results have been secured by the treatment of the colitis in those cases where it has been demonstrated.

Colitis Group. In addition to the 8 cases of catarrhal colitis and 2 cases of amebic dysentery in achylia subjects the series showed 16 cases of chronic catarrhal colitis, 6 cases of non-amebic ulcerative, colitis, and 5 cases of amebic ulcerative dysentery. The appearance of macroscopic mucus is not in itself sufficient evidence of a catarrhal condition. Mucus is essentially a protective substance, and is secreted when the mucosa is irritated. It seems to me the diagnosis rests on the history of repeated acute attacks of colitis, the presence of persistent tenderness over the course of the colon, the persistent admixture of mucus with or without pus and blood cells in soft feces, and the appearance of the mucosa of the rectum and sigmoid colon.

The diagnosis of amebic ulcerative colitis is best made by examination of scrapings made directly from the ulcerated areas with a dull curet. (In private and hospital practice I have repeatedly seen this demonstrated in cases of amebic dysentery when the report of the stools has been negative). Ulcerative non-amebic dysentery is comparatively rare in New York, according to my experience. Study of these cases has failed in every instance to demonstrate organisms of the dysentery group, although H. Strauss, of Berlin, in a recent article, reports positive agglutination findings with various bacilli of the typhoid dysentery group.

My experience with the treatment of the cases in which chronic colitis of various kinds has been demonstrated has been highly satisfactory. In the catarrhal cases I rely on a massive dose of bismuth subcarbonate, 3 ounces once a week, and daily rectal

injections of 8 to 16 ounces of a 10 per cent. solution of gelatin given at a temperature of 116° to 125° F. A diet rich in cellulose or the hemicellulose, agar-agar, is a most important means of preventing a recurrence of the catarrhal conditions. These cases have all done well with few exceptions in spite of gastric conditions. In the past six months I have seen two remarkable successes in intractable bloody dysentery of a severe form by the use of a preparation of the phenol group which the maker calls "trimethyl-methoxyphenol." It is said to be twenty times more bactericidal than carbolic acid, and its use in doses of 40 minims daily gives no evidence of toxicity, as it is not absorbed from the intestinal tract in the smallest amount. A rapid and permanent cure of these ulcerative dysenteries has been brought about by administration of this product by mouth and the addition of this preparation to gelatin injections. In my three previous cases of severe chronic bacillary dysentery the ultimate results were bad.

Emotional Diarrhea Group. Neurotic conditions, as an explanation for chronic diarrhea are highly unsatisfactory, and only twice in this series have we been satisfied with this explanation It is true that in many instances the patient is of a nervous temperament or has an irritable nervous system, and in one way or another this may increase the tendency to diarrhea. On the whole, however, such a diagnosis we would regard as exceedingly untrustworthy unless every other cause could be excluded and there was a most intimate association between exaggerated emotional states and abnormal peristaltic activity of the colon.

Stasis Group. A definite group or groups of cases complaining of diarrhea may with modern methods of diagnosis, especially the Roentgen-rays and sigmoidoscope, be found to have an underlying colonic stasis. Clinically, it has seemed to me we have three fairly well-marked varieties of this condition. This has been the sole condition found in 8 cases, and in all the diarrhea has been cured by treatment of the underlying constipation.

The first is a group of patients, usually young women, complaining of diarrhea, although the stools on examination are found to consist of small balls, apparently spastic feces. Examination of the sigmoid, in spite of several previous movements during the morning, shows a considerable filling with well-formed feces in the form of these tiny balls. Apparently we have to deal with a spastic irritability of the lower colon and a failure to empty the bowel completely at one time. Some of these cases are attended with an abnormal tightness of the sphincter muscle, with or without irritable fissures or hemorrhoids. On one occasion a single polyp was found high in the rectum, the removal of which resulted in the cessation of this rectal irritability.

The second group of cases may properly be designated fecal impaction, and fluoroscopic or roentgenographic examination shows

a dilated colon with a passage through a portion of the impacted area. This type of stasis constipation has been seen three times in this series, always in patients well along in years and of rather corpulent habit.

The third group is one which we have begun to recognize since using the Roentgen-rays as a routine in the study of these cases. There is stasis in a dilated cecum, usually prolapsed over the brim of the pelvis, which retains its contents an abnormal time—fermentative processes may be set up which give rise to intermittent or persistent diarrhea. It seems quite probable that this is one of the causes of the condition described by Schmidt and Strassburger as Gärungsdyspepsia and Gärungcatarrh. It is possible that diarrheas which have been said to depend on chronic appendix conditions are in reality brought about by conditions other than the inflamed appendix in the right iliac fossa. Diarrhea associated with chronic appendicitis is decidedly rare, and in those cases which have come under my observation it has persisted in spite of appendectomy, but has been relieved by the treatment of the coincidentally inflamed mucosa of the colon.

Thyroid Group. In 9 cases there was ample evidence of hyperthyroidism, 4 showing definite exophthalmic goitre. As a rule, these patients do not seek relief for the intestinal disturbance but consult a heart specialist or neurologist. From my study of these cases I am convinced that we have to deal simply with hyperperistalsis, without failure of gastric or intestinal digestion, without colitis, without stasis. Every chronic diarrhea in a neurotic subject should be under suspicion of having its origin in a disturbance of thyroid function, and careful search should be made for the characteristic signs associated with hyperfunction of the gland.

Pancreatic Group. Chronic pancreatitis and cancer of the pancreas with or without obstruction of the common bile duct are usually attended with large, soft, fatty stools, but by no means with diarrhea. In only one case in this series was chronic change in the pancreas demonstrated, and in this instance the condition was extremely severe, attended with glycosuria, with a high grade of intestinal putrefaction and colitis. I doubt that failure of pancreatic digestion is ever an adequate explanation of persistent diarrhea.

Adrenal Group. Five cases in this series have seemed to me to represent an incipient form of Addison's disease, characterized by marked secondary anemia, with high lymphocyte count, disproportionate loss of flesh and strength, low blood-pressure, and a slight general bronzing of the skin without definite changes in the mucous membranes. In all of these cases it was possible to exclude thyroid disease, colonic stasis, failure of gastric digestion, and colitis. In 3 of these cases excellent results were secured by the use, over a long period, of nucleoproteid of the adrenal made by

Dr. S. P. Beebe, of Cornell University. Other adrenal preparations failed to have any effect on the diarrhea.[3] We have tried out this preparation in diarrheas apparently due to other conditions without success. Adams in his analysis of 97 cases of Addison's disease found that 31 showed definite improvement with a preparation of the adrenal gland given by mouth, while 16 were permanently relieved. We are, of course, dealing with an indefinite and complex group of cases, and the mere fact that these patients have survived for some years may throw some doubt on the suggestion of their having had disease of the adrenal gland. It is possible that we had to deal with a disturbance of adrenal function without actual destruction of the gland. The fact remains, however, that this preparation of the gland substance was specific in these 3 cases, while in general it has no constipating tendency.

SUMMARY. 1. Chronic diarrhea is a relatively infrequent affection. It may complicate any morbid condition, but in the study of this series of cases the attempt has been made to determine the factors responsible for the disturbance of bowel function.

2. Achylia gastrica occurs in about one-third of all cases, but is to be regarded as a predisposing cause of irritation and inflammation of the colon. The most satisfactory results in diarrhea associated with achylia were obtained by the treatment of colonic stasis by diet and the colitis by appropriate measures.

3. Colitis is not necessarily accompanied by chronic diarrhea, but particularly in the nervous seems to give rise to irritability of the colon, which causes frequent evacuations.

4. Colonic stasis may give rise to chronic diarrhea, and dietetic measures which increase peristaltic activity quiet the apparently already overstimulated bowels. Stasis is probably an important predisposing factor in colititis, for the permanent relief of the colitis depends largely on overcoming stasis.

5. Emotional excitability may at times be a factor in causing diarrhea, but nervous states are rarely to be regarded as the sole cause of chronic looseness of the bowels.

6. Hyperthyroidism frequently gives rise to a chronic diarrhea of moderate severity. It differs in this particular from the severe diarrhea, attended with emaciation and prostration, which accompanies destruction of the adrenal gland. It seems quite probable that the latter condition is more common than has been recognized, and is not entirely dependent on the destruction of the gland substance.

7. Success in the treatment of chronic diarrhea is peculiarly dependent upon the exhaustive study of the case by all diagnostic resources, particularly as a combination of factors is not infrequently responsible for the normal activity of the bowel.

[3] Practitioner, Oct., 1903, p. 473.

THE METABOLISM IN A CASE OF MYASTHENIA GRAVIS, WITH CONSIDERATIONS ON THE ADMINISTRATION OF CALCIUM AND OF GLANDULAR PREPARATIONS.

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A number of clinical and pathological observations in cases of myasthenia gravis have caused various authors to assign a prominent pathogenetic role in this disease to one or another of the organs of internal secretion as well as to the liver.

Oppenheim was the first to report a lesion of the *thymus* in this disease. In another case, Weigert found a lymphosarcoma of the thymus, associated with cellular infiltrations in the muscles, which he ascribed to metastases from the thymus tumor. A number of other cases have been reported in which some abnormality of the thymus was found at autopsy. Mandlebaum and Celler[2] have reported such a case, and in their excellent review of the subject are inclined to consider neoplasms of thymus origin as a possible pathogenetic factor in a certain proportion of the cases. A number of therapeutic suggestions have been based upon this association. Schuhmacher[3] claimed to have secured marked improvement after thymectomy in a case of Basedow's with myasthenic symptoms.

The association of myasthenia with *Basedow's* is not an uncommon one. Stern[4] in a recent article has cited a number of cases showing it. In his own case, tetanoid contractions of the fingers and pigmentation and bronzing of the skin were later associated with these conditions. He proposes to treat the disease by complete thymectomy and unilateral thyroidectomy.

Chvostek[5] ascribes importance to disturbances of the *parathyroids*. He attributes myasthenia to hyperfunction or dysfunction in contrast to the hypofunction of this gland, which he assumes to be the cause of tetany. The changes in the thymus so frequently found in myasthenia, he believes are of no pathogenetic

[1] Work done under tenure of the Theodor Escherich Fellowship in Pathology.

[2] Jour. Exp. Med., 1908, x, 308.

[3] Mitt. a. d. Grenzgeb. d. Med. u. Chir., vol. xxv.

[4] Neurol. Centralbl., 1914, p. 409.

[5] Wien. klin. Wchnschr., 1908, xxi, 37; Lubarsch and Ostertag's Allg. Pathol. u. pathol. Anat. d. Mens. u. Tiere, 1908.

importance. The weight of experimental evidence is against his theory.[6]

We have referred to the finding of bronzing and pigmentation of the skin in myasthenia by others. This was present in our case as well. It is well known that in dogs muscular weakness and increased skin pigmentation follow adrenal extirpation and that the pigmentation can be made to disappear by infusions of epinephrin. Therefore, an etiological connection between an *adrenal* lesion and the myasthenic symptom-complex must be considered possible. The high blood-pressure in our case might also be taken as further evidence of this connection were it not that the experimental facts in regard to the connection between disturbances of blood-pressure and adrenal lesions are contradictory.

The urine in our patient showed signs of a nephritis, the quantity and specific gravity were approximately normal, and the nitrogen excretion was sufficient. We are inclined to believe that the kidney lesion was comparatively unimportant and not in itself sufficient to explain the high blood-pressure.

At the time our investigations were made, previous publications on the subject led us to expect distinct variations from the normal in the metabolism of our patient. Spriggs[7] had found the creatinin excretion decidedly below normal in his patient. Pemberton[8] was able to corroborate this in one case, in which he found also a marked loss of calcium with a normal nitrogen balance. Diller and Rosenbloom[9] have quite recently published a case in which they got the same results for calcium and creatinin, accompanied, however, by a negative nitrogen balance. Kaufmann[10] in his patient investigated principally the nitrogen metabolism and the ammonia excretion. He found that exercise caused a decrease in the retention of nitrogen, and if continued, a loss together with increased excretion of ammonia. In his case there was, however, disease of the liver.

In our case the metabolism of nitrogen, phosphorus, sulphur, calcium and magnesium, and the ammonia and creatinin excretion were studied while at rest, with exercise to the point of exhaustion, during the administration of epinephrin (Parke, Davis & Co.), and of thymus[11] gland, followed immediately by a control period and also with prolonged administration of calcium. The calcium was given with the intention of studying its effect on the symptoms and on the loss of calcium we anticipated in the earlier periods. We wished to observe the effect of epinephrin and of thymus on the clinical symptoms and on the metabolism.

[6] Biedl, A., Innere Sekretion, 2d ed., 1913, i, 108.

[7] Quart. Jour. Med., 1907, i, 68.

[8] Amer. Jour. Med. Sci., 1910, cxxxix, 816. In Pemberton's work the composition of the food was obtained by computation, not by analysis.

[9] Amer. Jour. Med. Sci., 1914, cxlviii, 65.

[10] Monatsch. f. Psych. u. Neur., 1906, xx, 209.

[11] This and the other glandular substances given were Armour & Co.'s preparation.

A study of the tables shows that in our case, except for the creatinin, there was no striking variation from the normal in any of the constitutents studied during any of the experiments. There was throughout a retention of calcium, of magnesium, and of sulphur, and except for a very slight loss in the last period, a substantial retention of nitrogen and phosphorus. There was no disturbance of the ammonia excretion even during the exercise period (Period II), although at this time there was less retention of nitrogen. There is, therefore, contrary to the opinion held by Kaufmann, no evidence of an acidosis in our case. Period IV shows a slight increase in the retention of all the constituents. This was probably due in part to poor marking off of the stool, as the daily weight of the dried feces was less than in the other periods. During thymus feeding there was an increased retention of nitrogen and of phosphorus. Three days before the beginning of the period of calcium administration (Period X) the patient had a slight intestinal disturbance for two days, accompanied by abdominal cramps and diarrhea. It is probable that the slight loss of nitrogen and phosphorus is connected with this. During this period almost all of the additional calcium fed to the patient was excreted.

In common with previous observers we found a low creatinin excretion. This shows best in the creatinin coefficient, which averages 4.8 mgs. creatinin-nitrogen per kilo (normal 7–11 mgs.), while the ratio excreted to the total nitrogen averages 3.6 per cent., (normal 3.9 per cent.). During the thymus period and the calcium period creatin was excreted in noticeable amounts.

The work of Halpern has been made available to us very recently by a translation which we owe to the kindness of Dr. Lowenthal. In two cases of myasthenia, Halpern found marked retention of nitrogen, phosphorus, and lime, with a normal ammonia excretion. In his last published case,[12] during a five-day experiment, the daily intake (the composition of the diet appears to have been computed) and balance were as follows:

	Intake.	Retention.
Nitrogen	17.30 gms.	3.00 gms.
Phosphorus	2.40 gms.	0.13 gm.
Calcium oxide	3.65 gms.	1.69 gms.

The retention, it will be seen, closely resembles our results, except that the calcium retained by his patient is very much greater than in our case. The weight of the woman on whom the experiment was made is not mentioned, nor are any other clinical data given in his paper. In the absence of these it would be idle to attempt to explain the quantitative differences between his results and our own.

Prolonged administration of calcium, of ovarian substance, of

[12] Halpern, Miecz. Medycyna, 1912, xlvii, 914.

testicular substance and of thymus had no apparent effect on the clinical course in our case. While the patient was receiving epinephrin she developed cardiac palpitation and tachycardia after each administration, together with flushes and a feeling of weakness. It is clear that the result of our work offers no support for the administration of calcium in the treatment of this disease, as suggested by Pemberton. In the absence of clinical improvement from the administration of thymus gland, the increase in the retention of nitrogen and phosphorus do not constitute an argument for its use. Nor have we any evidence upon which to recommend the use of ovarian or testicular substance, while the use of epinephrin was clearly harmful in our patient.

CLINICAL DATA. S. S., aged forty-nine years; female. Admitted to the neurological service of the Mount Sinai Hospital, May 2, 1912.

Has one child alive and well. No other pregnancies. Last menstruation October, 1911. For the past two years troubled by epigastric oppression coming on a few minutes after eating and persisting for several hours, accompanied by eructations of gas. Has lost twenty-two pounds in last two months. About six weeks before admission she noticed drooping of right eyelid and inability to raise it at will, followed shortly after by the same manifestations in the left lid. At this time she once fell to the ground from weakness. About ten days before admission she noticed difficulty in swallowing, which became more and more marked toward the end of the meal. About three days later she noticed difficulty in speaking and feeling of heaviness and thickness in the tongue. The arms are gradually becoming weaker; the muscles of the neck have been weak since the onset of illness.

Physical Signs. Looks prostrated; sallow; skin negative.

July 5. *Eyes.* (Dr. Wolff). Incomplete ptosis of right eye; ocular motility in all directions restricted in varying degree, involving third, sixth, and fourth nerves of both sides. Lower branches of left facial nerve paretic. Fundi normal. Diagnosis: incomplete external ophthalmoplegia.

Very slight rigidity of neck. Teeth carious; pyorrhea alveolaris.

Lungs. Percussion note hyperresonant. Respiratory murmur distant and weak; expiration is low pitched and prolonged. Few moist rales at bases.

Heart. Rapid. First sound has lost most of its muscular quality. No enlargement.

Liver and Spleen. Negative.

Abdomen. Lower poles of both kidneys felt; otherwise negative.

Extremities. Inexhaustible clonus in right ankle. Deep reflexes generally exaggerated.

Sensations. Normal. Speech slow and difficult; enunciates poorly. Pronunciation of labials good, that of linguals somewhat impaired.

Swallowing difficult, no regurgitation through nose. Apparently some paresis of soft palate.

July 8. Less drooping of right eyelid. Voice stronger. Tongue can be fully protruded. Pulse of good quality and tension. The condition varies from day to day; at times voice becomes very weak and husky; eyelids droop and she says it is difficult to masticate because of weakness of lower jaw. No true fibrillation of tongue. Diagnosis at present between myasthenia gravis and organic bulbar-pontine lesion, with a probability of its being the former.

July 18. General condition improving; musculature becoming stronger. Speaks very much more clearly; can control eyelids with more power. Formerly when taking fluids by means of siphon tube, had to rest after an ounce or two. Now takes several ounces without resting. Pulse tension better. Her condition does not vary so much from day to day.

July 27. Electrical reaction. No reaction of degeneration. Muscles respond promptly to normal faradic current and rapid stimulation causes no fatigue. Patient thinks that power in hands is much improved after stimulation. On raising the arms at right angles, myasthenic reaction becomes very marked.

August 9. Myasthenic reaction in masseter, facial muscles, triceps, and pectoralis major marked.

August 27. Still partial ptosis of right eye, varying from day to day and at various times of same day. Feels much better. The exhaustion on voluntary movement no longer perceived. Voice less nasal. No dysphagia, no diplopia, etc. Since yesterday, slight exhaustion in supporting extended upper extremities.

September 13. Gradually improving. Ptosis and muscle exhaustion still occur at times. From this time until the patient left the hospital in January, 1913, there was no important change in her general condition. The myasthenic condition at times becomes more pronounced for a short period. In December bronzing of the skin was noted. This gradually increased and was most marked on the knees and elbows. There was no pigmentation of the mucous membranes. Several times during her stay in the hospital the bowels were loose for several days at a time. This condition yielded readily to treatment with opium and bismuth. Twice peculiar attacks were noted. These lasted fifteen to twenty minutes. She suddenly became very weak, dyspneic, broke into a cold sweat. The face and hands became cyanotic. The pulse was rapid, weak, and apparently low tension, but remained regular. Respiration was of the abdominal type, the chest being practically motionless.

Urine: Sp. gr., 1012 to 1026. Most of the examinations showed a faint trace of albumin, an occasional hyaline cast in the centrifuged specimen; no sugar. Daily quantity, 425 to 1100 c.c.

Wassermann and *von Pirquet* negative.

Blood Count. Leukocytes, 9000; small lymphocytes, 21 per cent.; large lymphocytes, 7 per cent.; eosinophils, 3 per cent.; polynuclears, 70 per cent.

Blood-pressure (summarized from several observations). Systolic, 190 to 215; diastolic, 140 to 170. Pulse pressure, 35 to 65.

The weight varied between 48.5 and 51 kilos.

The patient has been under observation since discharge from the hospital.

In March, 1913, diffuse pigmentation of buccal mucous membrane appeared. The strength of the muscles of the neck improved, but her condition otherwise remained unchanged. There was from time to time a transient improvement in her condition, so that she was able to walk about the room with assistance and at times alone.

Early in 1914 there was a period of marked improvement lasting six months continuously. Since September, 1914, at intervals of about a month, she became worse for a few days at a time. The muscles, especially of tongue, mouth, and eyelids, then became weaker; she felt generally weaker and had repeated flushes. During these periods she had a sensation of epigastric oppression, and the liver was tender and palpable. On several occasions there was nausea. Reflexes remained unchanged. The systolic blood-pressure was between 160 and 200. Thymus gland was given at home for two months immediately after the patient left the hospital. During the past two and a half years she received ovarian substance on and off for long periods, 5 grains being given three times daily. Dried-beef testicle was also given in the same dose for eight or nine months.

The patient died March 21, 1915, as the result of an acute bronchopneumonia. An autopsy could not be performed.

To sum up the clinical features, we have a characteristic case of myasthenia gravis presenting also an occasional transitory attack of marked dyspnea and tachycardia. Unusual symptoms are the extremely high blood-pressure and the increasing dermal pigmentation and pigmentation of the buccal mucous membrane.

Experimental Data. The patient during each of the metabolism periods and for at least three days preceding was fed on the Folin[13] test diet. The amount taken was carefully measured and an equal amount preserved daily for analysis. This was shaken with about 1 per cent. of toluol, placed on ice, and a combined sample made up for analysis at the end of each period. Urine and feces were also analyzed for the whole period, except that nitrogen, ammonia, creatin, and creatinin estimations in the urine were made for each day separately. Feces were marked off by means of carmin. All analyses were made in duplicate, and

[13] Amer. Jour. Physiol., 1905, xiii, 45.

the figures given are averages from pairs of closely corresponding results. The analytical methods used have been given in detail by one of us in an earlier paper,[14] the only variation being that feces, food, and urine were all ashed in platinum as a preliminary to the McCrudden method. Except during Period II the patient was kept in bed.

Period I. Duration, six days—July 24 to 30.

Period II. Duration, six days—August 1 to 7. Walked several times a day until exhausted; aggregate about 500 meters daily.

Period IV. Duration four days—August 14 to 17. From August 11 to 17 inclusive, 10 minims of 1-1000 epinephrin were given hypodermically three times daily.

Period VI. Duration six days—September 1 to 7. Five grams of thymus gland were given thrice daily during this time.

Period VII. Duration, seven days—September 7 to 14. Thymus gland was given from September 14 to November 18 in the same dose as before. From November 15 to December 26, 6 gms. of calcium lactate were given daily in four doses.

Period X. Duration six days—December 18 to 22. On account of slight intestinal disturbance preceding it the food mixture was diluted with half its volume of water. The calcium lactate contained 0.7734 gms. CaO in the daily dose. The feeding mixture also contained more lime than before, so that the amount of this substance given was about double that during the other periods studied.

The results of the analyses follow and are averaged for each period in grams per diem:

TABLE I.

Period.		I	II	IV	VI	VII	X
Food	N	8.082	8.86	9.32	9.86	9.75[15]	9.87
	S	0.791	0.876	0.938	0.952	1.048	1.238
	P	0.805	0.999	0.948	1.037	1.033	1.037
	CaO	1.084	1.137	1.145	1.18	1.112	2.207
	MgO	0.299	0.336	0.339	0.328	0.409	0.331
Feces	N	0.443	0.766	0.255	0.997	0.755	0.8
	S	0.042	0.067	0.038	0.098	0.072	0.105
	P	0.175	0.223	0.114	0.246	0.18	0.328
	CaO	0.511	0.939	0.371	0.767	0.62	1.548
	MgO	0.082	0.245	0.102	0.174	0.137	0.213
Urine	N	5.377	7.07	6.335	5.441	6.659	9.458
	S	0.616	0.495	0.569	0.518	0.605	0.765
	P	0.602	0.622	0.446	0.472	0.611	0.899
	CaO	0.128	0.136	0.112	0.192	0.192	0.34
	MgO	0.045	0.039	0.06	0.076	0.08	0.109
Balance	N	+2.262	+1.023	+2.73	+3.422	+2.336	−0.388
	S	+0.133	+0.314	+0.34	+0.336	+0.371	+0.368
	P	+0.028	+0.154	+0.386	+0.319	+0.242	−0.19
	CaO	+0.455	+0.062	+0.662	+0.221	+0.3	+0.319
	MgO	+0.172	+0.052	+0.176	+0.078	+0.192	+0.009

[14] Bookman, A., Amer. Jour. Dis. of Children, 1914, vii, 436.

[15] Computed.

TABLE II.

Period.	I	II	IV	VI	VII	X
Total nitrogen	5.38	7.07	6.33	5.44	6.66	9.46
Ammonia nitrogen	0.42	0.396	...	0.367	0.466	0.556
Creatin	0.046	0.036	...	0.148	.....	0.202
Total creatinin	0.653	0.571	0.71	0.613	0.518	0.805
Total creatinin as nitrogen	0.242	0.212	0.26	0.227	0.192	0.299
Percentage of total creatinin, nitrogen to total nitrogen	4.5	3.0	4.1	4.2	2.8	3.2
Milligrams of creatinin nitrogen per kilo body weight	4.7	4.1	5.1	4.7	4.0	6.0

SUMMARY. This case of myasthenia gravis presented as unusual symptoms bronzing of the skin and pigmentation of the buccal mucous membrane and high blood-pressure.

The metabolism of calcium, magnesium, phosphorus, sulphur, and nitrogen and the ammonia excretion were studied, with the patient at rest, while taking exercise, during the administration of epinephrin, of thymus gland, and of calcium, and presented no abnormal features. The excretion of creatinin was below normal. There was at times a considerable excretion of creatin.

Ovarian and testicular substance were also administered. Neither the glandular preparations nor the calcium appeared to have any influence upon the clinical course.

REVIEWS

PRINCIPLES OF HUMAN PHYSIOLOGY. By ERNEST H. STARLING, M.D. (Lond.), F.R.C.P., F.R.S., HON. M.D. (Breslau), HON. Sc.D. (Cambridge and Dublin). Second edition; pp. 1271; 566 illustrations, 10 in colors. Philadelphia and New York: Lea & Febiger, 1915.

PERHAPS none of the fundamental subjects in medicine has undergone more radical changes of late than has physiology. For this reason it is particularly gratifying to welcome a new and thoroughly revised edition of Starling's *Text-book of Physiology*, long regarded as one of the standard works on this subject.

In this new edition the author has wisely eliminated some of the less important subjects that appeared in the first edition, thereby reducing somewhat the size of the volume. At the same time, however, he has brought the subject matter thoroughly up-to-date by revising and even rewriting many of the sections and by introducing much new material. Among the chapters that have been decidedly improved by rewriting, are those on the circulation and those on the voluntary muscles. The additions embrace invariably live subjects that have proved to be of far-reaching importance and wide-spread interest. For example Starling discusses carefully such topics as vitamines, the human cardiogram, the various cardiac nodes, etc., and has added entire chapters dealing with the innervation of the bronchial musculature and the nutrition of the brain. To enumerate in detail all the additions and changes is out of the question. Suffice it to say that in this new edition, the author has set forth that which is best and most modern in physiological teaching.

Throughout the entire book one is impressed by the fact that Starling never fails to emphasize the fundamental relationship that exists between physiology and the clinical side of medicine. As a result of this attitude he has introduced into physiology a clinical interest that should prove helpful and stimulating to both student and practitioner. G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics in the Jefferson Medical College, Philadelphia, and LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics in Jefferson Medical College, Philadelphia. Vol. III, September, 1915. Pp. 307; 26 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

IN *Progressive Medicine* for September, 1915, William Ewart has a most instructive article of nearly a hundred pages on the heart, lungs, and other intrathoracic viscera, including the thyroid. Ewart's medical contributions have distinct literary merit; like many of his countrymen he takes the trouble to write well, thereby setting an example that might to advantage be followed by a large number of present-day medical writers. Ewart in this contribution has not confined himself to purely clinical subjects, but has taken up at some length many important physiological and pathological problems. Dermatology and syphilis are discussed by William S. Gottheil. He lays particular stress upon the treatment of psoriasis, furunculosis, dermal tuberculosis, and favis and ringworm of the nails. The few pages he devotes to syphilis are almost wholly taken up by a discussion of the present status of syphilis therapy. As has always been the case heretofore, Edward P. Davis furnishes a most exhaustive review of obstetrics. In addition to discussing pregnancy, eclampsia, the placenta, labor, and the puerperium, he devotes considerable space to obstetric surgery and to diseases of the newborn. The article on diseases of the nervous system, which concludes the volume, is worthy of its eminent author, William G. Spiller. Without placing undue emphasis on any one subject, in the space of fifty-eight pages Spiller seems to have touched upon nearly every new and important subject in neurology. G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics in Jefferson Medical College, Philadelphia, and LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. IV. December, 1915. Pp. 421; 79 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

VOLUME IV, the December number of *Progressive Medicine*, opens with a long article by Edward H. Goodman on diseases of the digestive tract and allied organs. At the outset he lays great

stress on oral sepsis and its relation to disease. Among the many other important subjects which he particularly emphasizes should be mentioned: studies on gastric function; gastric ulcer and carcinoma; achylia gastrica; syphilis of the stomach; duodenal ulcer; constipation; colitis polyposa; chronic appendicitis; functional tests for hepatic insufficiency; cholelithiasis; pancreatitis; and pancreatic functional tests. J. Harold Austin's contribution on diseases of the kidneys is an admirable critical review of the enormous amount of work that has recently been done on renal function. In addition, he describes various types of nephritis, uremia, renal tuberculosis, and hydronephrosis. The surgical aspect of renal diseases is dealt with by Charles W. Bonney, who also takes up diseases of the ureter, bladder, prostate, and genito-urinary diseases in general. Of the many noteworthy contributions that each year appear in *Progressive Medicine*, there are none more deserving of favorable comment than the careful, critical reviews furnished by Joseph C. Bloodgood. His present article, dealing as it does largely with the subjects of shock, anesthesia, wounds, infection, fractures, and dislocations, is particularly interesting, since it has given him an opportunity to describe first aid and military surgery, with special reference to the lessons learned in the present European conflict. The volume concludes with a practical therapeutic referendum by H. R. M. Landis, in which he discusses many therapeutic agents that are of particular interest at present, such as the various sera, benzol, corpus luteum crotalin, emetine, kaolin, liquid paraffin, pituitrin, and vaccines.

Without a doubt, each year the contributions to *Progressive Medicine* are more thoughtfully and carefully prepared; the result is that with every new volume this quarterly becomes more and more a necessity to the physician who strives to keep abreast of the times.

G. M. P.

NOTES ON DENTAL METALLURGY. By W. BRUCE HEPBURNE, L.D.L. (Glasgow), Lecturer on Dental Metallurgy and Visiting Dental Surgeon in the Glasgow Dental College and School; Member of the Dental Examining Board of the Royal Faculty of Physicians and Surgeons. Second edition. New York: William Wood & Company.

THE present revised edition of this book which the editor now presents is a valuable contribution to dental metallurgy, and was probably prompted by the manifest changes in the knowledge and views now held regarding amalgams and cements. The chapters devoted to these subjects and alloys clearly and ably express the most recent ideas. The field that obtains strictly to dental metallurgy is important but rather restricted. This small book has been most carefully written throughout, and can be recommended.

P. L. L.

THE HOUSE-FLY, MUSCA DOMESTICA LINN. ITS STRUCTURE, HABITS, DEVELOPMENT, RELATION TO DISEASE AND CONTROL. By C. GORDON HEWITT, Dominion Entomologist of Canada; formerly Lecturer in Economic Zoölogy in the University of Manchester. Pp. 382; 104 illustrations, partly in colors. Cambridge University Press, Zoölogical Series.

THIS work represents the development of a subject which was presented by the author in a series of papers during the years of 1907, 1908, 1909. It is not designed to be a popular treatise on the house-fly, but is intended to serve the more exacting needs of "entomologists, medical men, health officers, and others similarly engaged." Doubtless it will be very welcome to those whose business it is to fight the diseases propagated by our most common insect pest. The scope of the book is indicated by the titles of its six parts. They are: (1) structure and habits of the house-fly; (2) breeding habits, life history, and structure of the larva; (3) the natural enemies and parasites of the house-fly; (4) other species of flies frequenting houses; (5) the relation of house-flies to disease; (6) control measures. Nearly one-third of the book is devoted to a consideration of the last two topics. Experiments showing the nature of the dissemination of various disease-producing bacteria are described and illustrated. Practical means for reducing the numbers of flies are considered. There is an excellent bibliography, together with author and subject indexes. C. E. McC.

A TEXT-BOOK OF MEDICAL CHEMISTRY AND TOXICOLOGY. By JAMES W. HOLLAND, M.D., Emeritus Professor of Medical Chemistry and Toxicology, Jefferson Medical College, Philadelphia. Fourth edition; pp. 678; 116 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE problem confronting every author of a text-book is to keep its successive editions abreast of the times. Although but four years have passed since the third edition of Holland's *Medical Chemistry and Toxicology* appeared, still many new changes were necessitated in the revision of the present work.

The rapidity with which we are making progress in these fields is indicated by an increase of 147 pages over the previous volume. With the exception of the opening paragraphs, which have been omitted, the first 245 pages are practically unchanged; in fact, the same general plan of the previous edition has been continued in this fourth printing; one which seems most satisfactory. Extensions to the chapters on radium, thorium, uranium, and vanadium cover the field very well. The newer organic compounds of arsenic,

the constitution of the carbohydrates and glucosides, the synthetic local anesthetics allied to cocain, the protective enzymes, the hormones, and an entire new chapter on feces are all subjects of timely and valuable information to the reader. A number of new tests have been added, including those in connection with names of Seleivanoff, Wassermann, Volhard, Harvey, Benedict, Folin, Hart, Russo, Tsuchiya, Fromer, Abderhalden, etc. Whether all of these tests should occupy a position in a standard text-book is of course open to debate. Some of them still operate on uncertain grounds. A more minute description of the details in their execution would, we believe, be of value to the student of medicine who goes to this book as a laboratory guide.

The work remains an excellent exposition of the subject. It covers the ground in a crisp manner and furnishes a foundation for those who choose to build upon it. The author is to be congratulated upon the revision. T. G. S.

ROENTGEN RAYS: HOW TO PRODUCE AND INTERPRET THEM. By HAROLD MOWAT, M.D. (Edin.), Temporary Lieutenant R. A. M. C. At present Officer to Roentgen-ray Department, Meerut Indian General Hospital; Radiographer to Metropolitan Hospital and Royal Chest Hospital. Pp. 204; 106 illustrations. New York: Oxford University Press, 1915.

IT is unfortunate that this book should have gone to press just at this time, when the author's military service has evidently been the cause of its completion in a very hurried manner. He states in the preface that the "book is written for those who have little or no knowledge of the subject of Roentgen rays." Unfortunate, again, since it is for this class of readers that the greatest accuracy is essential, and the book is certainly not free from inaccuracies, in addition to being very incomplete. We cannot conscientiously recommend it to this class of readers, to say the least. The criticism of a roentgenologist would begin at the title and continue to the end. The illustrations in connection with the thorax and digestive tract are exceedingly poor. H. K. P.

HEADACHE. By DR. SIEGMUND AUERBACH, translated by ERNEST PLAYFAIR, M.B., M.R.C.P. Pp. 208. London-Oxford University Press.

THIS small volume is a splendid scientific discussion of the important symptom of headache in all its various phases and manifestations. It well merits a careful study. H. J. M., JR.

HUMAN PHYSIOLOGY. By LUIGI LUCIANI, Director of the Physiological Institute of the Royal University of Rome. Translated by FRANCES A. WELBY. In five volumes. Vol. III. The Muscular and Nervous Systems. Edited by GORDON M. HOLMES. M.D. Pp. 558; 141 illustrations. New York: Macmillan Company, 1915.

THE third volume of the monumental work of Luciani excels the two volumes which have previously found their way into English on account of the fact that the translation is from the fourth Italian edition, which has appeared since the English translations of Volumes I and II. The subject matter is thus brought up to 1913.

The book embraces the following subjects: general physiology of muscle; mechanics of the locomotor apparatus; phonation and articulation; general and special physiology of the nervous system. At the end of each chapter is a short bibliography containing only most carefully selected references. References to recent English literature have also been introduced. The volume, therefore, on account of the thoroughness with which the subjects have been considered and the brief but valuable bibliography, serves as a most splendid reference book.

In this volume, perhaps more so than in any of those which have thus far appeared, one appreciates the wonderful mentality of its illustrious author. The logical sequence of the data presented, the conservatism of opinion upon mooted subjects, the philosophical attitude both broad and analytical, and the clearness of expression, all impress the reader with his greatness. The work for years to come will remain a much-used book of reference, will live as do the works of Müller and those works edited by Schäfer. The reader is seldom conscious of being in the hands of a translator; the style is clear and free.

E. L.

AN ESSAY ON HASHEESH, INCLUDING OBSERVATIONS AND EXPERIMENTS. By VICTOR ROBINS, Contributing Editor, *Medical Review of Reviews;* Pharmaceutical Chemist, Columbia University. Pp. 83. New York: Medical Review of Reviews.

THIS essay on hasheesh is made the cloak for an interesting bit of observation and experimentation. The historical, pharmaceutical, and therapeutic considerations of the drug are followed by an account of the results of its administration, in intoxicating dose, to a number of persons, including the author himself.

A. A. H.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The European Bed-bug as a Carrier of Disease. — D. THOMSON (*Annals Trop. Med. and Parasitol.*, 1914, viii, 19) points out the advances made in the study of the transmission of such tropical diseases as malaria, yellow fever and filariasis. Similar work has, he says, been neglected in connection with diseases of the temperate climates. The present study deals with the European bed-bug. Thomson first studied 184 bugs as controls; the majority of them were adult bugs which had presumably fed upon human beings who may have been diseased, and were not, therefore, proper controls in the strict sense of the term; 107 of these were examined for acid-fast bacilli with the Ziehl-Neelsen stain, the remaining 77 being stained with Giemsa's stain. No acid-fast bacilli were found and no protozoa. In feeding the bugs on diseased individuals the following results were obtained: One hundred and five bugs fed on lepers and 35 caught on the matresses of lepers were examined. In none were acid-fast organisms found. Five bed-bugs were fed on an advanced case of Hodgkins' disease. All developed within eight days a gravish, mouldy growth over the body and examination showed them to be infected with a mycelium and spores. However, 22 bugs fed on an early case of Hodgkins' disease showed no such condition, even thirteen days after feeding, though 65 per cent. of them showed "Chlamydozoön-like bodies." Thirty bugs fed on a patient with myeloid leukemia were studied, the examinations being made four to nineteen days later. All showed Charcot-Leyden crystals in intestines and feces. Fifty per cent. of these bugs also contained the "Chlamydozoön-like bodies." The latter were also found in 60 per cent. of the bugs which fed on a patient with lymphoid leukemia and in 43 per cent. of those allowed to feed on a

patient with sarcoma of the ileum. The results with a few bugs fed on a cancerous patient were entirely negative. While Thomson's results are largely negative, there is need for further study, he says.

The Relation of Bile Pigments to Hemoglobin.—J. O. W. Barratt and W. Yorke (*Annals Trop. Med. and Parasitol.*, 1914, viii, 509) have made an experimental study on the rabbit of the relation of bile pigments to hemoglobin. Under ether anesthesia, a cannula was inserted into the gall-bladder; the common duct was ligatured. The bile was collected for a certain period of time and then homologous hemoglobin solutions were injected intravenously. The bile was again collected and its concentration was compared with that collected during the control period by means of a Zeiss comparison spectroscope. Barratt and Yorke summarize their findings as follows: Consequent upon intravenous injection of hemoglobin solution there is a distinct and immediate increase not only in the concentration of bile pigment but also in the amount of bile pigment excreted. During the three or four hours following the injection the amount of pigment excreted may increase from four to six times the amount found before the injection. Two hypotheses may be advanced to explain this increase, (1) that the hemoglobin injected is actually converted by the liver into bile pigment, or (2) that it merely stimulates the liver cells to increased production of bile pigment. Against the first hypothesis is the fact that the increase of pigment is not so great as might be anticipated from the relatively large quantity of hemoglobin introduced into the circulation and the consequent high degree of hemoglobinemia resulting (up to 20 per cent.). The amount of hemoglobin found in the plasma of normal rabbits is between 0.02 and 0.05 per cent. This fact seems to indicate that the degree of red-cell destruction normally occurring in the living animal is slight. Assuming that the pigment of normal bile is derived entirely from hemoglobin set free by the disintegration of erythrocytes normally occurring in the living animal, then it is rather surprising that when the degree of hemoglobinemia is increased four hundred times, the amount of bile pigment is augmented only sixfold at the most. Furthermore, as Yorke and Nauss have shown, the mere introduction of homologous hemoglobin solution into the veins of normal rabbits is not enough to produce jaundice. The hemoglobinemia gradually disappears, leaving the blood plasma clear and colorless without any trace of bile pigment. Barratt and Yorke attempt to apply their results to blackwater fever. Since from these experiments it appears that intravenous injection of hemoglobin results in an increased excretion of bile pigment it would seem that the icterus almost invariably observed in blackwater fever cannot be attributed solely to hemoglobinemia.

An Improvement in the Phenolphthalin Test for Occult Blood in the Feces.—I. Boas (*Deutsch. med. Wchnschr.*, 1915, xli, 549) describes a modification of his recently proposed method of performing the phenolphthalin test for occult blood in the feces. The reagent is prepared as follows: 25 gm. of potassium hydrate are dissolved in 100 c.c. of distilled water; 1 gm. of phenolphthalin is added, and the mixture is taken vigorously. After solution is complete, powdered metallic

zinc is added, and the preparation is boiled in an Erlenmeyer flask until the fluid is completely decolorized. After cooling, distilled water is added to the original volume and the solution is filtered. The filtrate is water-clear and remains colorless when acetic acid, alcohol and hydrogen peroxide are added to a portion of it in a test-tube. The solution is stable for several weeks. In the course of time oxidation of the phenolphthalin around the lip of the bottle may occur. It is always advisable to use a colorless solution. The method of performing the test Boas describes as follows: An acetic acid-alcohol extract (5 gtts. acetic acid and 15–20 c.c. alcohol) of the feces is prepared. From a dropping bottle 15 gtts. of the reagent are placed in a test-tube, to which are added 5–6 gtts. of 3 per cent. hydrogen peroxide and 2 c.c. of absolute alcohol. The tube is well shaken. The fecal extract is filtered and the filtrate is allowed to run slowly into the test-tube, so that it forms a layer with the prepared reagent, about one-half of the filtrate being employed. If blood coloring matter is present, there appears immediately or gradually a rose or deep red ring at the line of contact, the depth of color depending upon the amount of blood pigment present. If the color is faint, it is more readily perceived by placing the tube before a white background. The result of the test is rarely doubtful. But when such is the case, Boas proceeds in the manner devised by Schumm for increasing the delicacy of the guaiac test; the feces are rubbed up with equal parts of alcohol and ether, filtered repeatedly, and then the filtrate is evaporated to dryness. The dry residue is suspended in acetic acid-alcohol and filtered. Then, using the filtrate as the fecal extract, the method as described above is followed, when the rose-colored ring becomes definite if blood is present. Boas has carried out duplicate tests with guaiac and with benzidin. He has found the phenolphthalin test more delicate than the benzidin and much more sensitive than the guaiac. Furthermore, whenever he has found the guaiac and benzidin tests positive, the phenolphthalin test has always been plainly positive. The observations described above relate only to occult blood in the feces. With stomach contents the contents are different, and will be discussed in a subsequent communication.

Observations on Infection and Immunity in Maternal and Fetal Lues.—From his observations on large material of his own and from reports in the literature, J. TRINCHESE (*Deutsch. med. Wchnsch.*, 1915, xli, 555) has reached certain definite conclusions in regard to luetic mothers and their offspring, which he summarizes as follows: I. Colles' law is false, *i. e.*, an immunization of the mother by the fetus is impossible, because (*a*) a paternal infection of the fetus does not occur and (*b*) the fetus produces no immune bodies. II. Profeta's law is misleading. Immunization of the fetus by the mother does not occur, for the placenta is impermeable to the immune bodies of the maternal organism. III. The earlier the fetus is infected, the more rapidly the syphilis advances after the manner of sepsis, which leads to the death of the fetus within six weeks. IV. Until about the eighth month the fetus forms no immune bodies and its blood is therefore negative to the Wassermann reaction, though its tissues may be swarming with spirochetes and the mother's blood may yield a positive

Wassermann reaction. V. In the last month of pregnancy the fetus begins to develop protective substances and its blood may give a positive Wassermann test. VI. If the infection of the child occurs in the last few weeks before birth, clinical symptoms of lues at birth may fail and the Wassermann reaction may be negative, since the incubation period for both phenomena may have been too short. These are the children formerly looked upon as immune. They are, in reality, the "late" syphilitic children. VII. If, indeed, it happens that latent or even florid luetic mothers bear healthy children, then, in consequence of VI neither the lack of symptoms nor the negative Wassermann reaction is certain evidence that the child is healthy. VIII. The following are the possibilities at birth for the offspring of syphilitic mothers: 1. The child is clinically syphilis-free and has a negative Wassermann reaction. 2. The child is clinically syphilis-free and has a positive Wasserman reaction. 3. The child has clinical syphilis and a positive Wassermann reaction. 4. The child has clinical syphilis and a negative Wassermann reaction. In the sequence given, the possibilities for the life of the child become progressively worse, so that the fourth generally means the death of the child.

Vaccination Against Typhoid in the United States Army.—LYSTER (*Jour. Amer. Med. Assn.*, 1915, lxv, 510) says that for the decade 1900 to 1909 there were 3,510 cases of typhoid fever among the American troops, with an average therefore of 351 cases per annum. In 1909 up to September 1, 830 individuals had received one or more doses of the typhoid vaccine, a number which, for all practical purposes can be disregarded. In this year there were 282 cases of typhoid in the army consisting of a mean strength of 84,077. In the year 1910, 16,093 persons were vaccinated. One hundred and ninety-eight cases of typhoid are reported for the same year. In 1911 from January to June 30, nearly 28,000 officers and men were vaccinated. The routine vaccination of all recruits was begun in June, 1911, and on September 30, 1911, vaccination was made compulsory for the entire army. The gradual introduction of vaccination against typhoid began to show results as soon as it was done on a scale of any size. This was by the end of 1910. In that year, with 198 cases of typhoid fever, it can hardly be stated that the disease was "practically abolished" by improved sanitation, as the antivaccinationists would have us believe. By the end of 1911, seventy cases of typhoid fever had occurred. By the end of the first quarter of 1912, practically all of the army was vaccinated, and new men coming into the service were being vaccinated as soon as enlisted. There were twenty-seven cases to the end of that year and nineteen of these were in the persons of soldiers who had not been vaccinated against typhoid fever. When vaccination can be said to have become complete, as in 1913 and 1914, there were four and seven cases, respectively, and only two of these had had the complete course of vaccination when they were taken with typhoid fever. The standard of sanitation maintained has not varied noticeably for some years. The only change in recent years has been a system of conservancy in camps that largely prevents flies entering the latrines and becoming conveyors of disease. But this could have affected only a small part of our troops in any year. In

1911 from 10,000 to 12,000 out of a total of 92,802 were in camps; during the last two years (1913–1914), from 12,000 to 15,000 out of a total of 92,580. Finally it must be remembered that the soldier comes into quite as intimate contact with civilians as he does with his comrades. He contracts diseases (measles, mumps, scarlet fever, influenza and others) just as he did before, with the exception of smallpox and typhoid fever. Why are these diseases practically no longer existent among our soldiers? Vaccination against smallpox and against typhoid fever are the active agents in banishing these diseases from armies that thoroughly and efficiently use these measures. It may be of interest to add that for the first six months of 1915, only one case of typhoid has so far been reported as occurring in the United States Army.

SURGERY

UNDER THE CHARGE OF

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Gastrostomy for Stomach Drainage.—Nyström (*Zentralbl. f. Chir.*, 1915, xl, 721) says that Jaboulay, in 1905, employed the stomach fistula in a case of peritonitis with ileus to control the great distention of the abdomen and obtained a marked relief of the respiratory disturbance. The patient recovered. It has been employed with success in cases of volvulus of the small intestine and gastric dilatation. The direct permanent drainage of the stomach by gastrostomy is indicated especially in two kinds of cases: (1) In ileus. Through stomach drainage the intestinal contents streaming into the stomach are immediately and continuously being evacuated. The distention of the upper part of the abdomen is removed, the diaphragm can move more freely and the heart action and respiration do not suffer as when the diaphragm is forced upward. Vomiting ceases and the patient drinks freely without evil consequences. (2) In operations on the stomach, this procedure is indicated when a suture insufficiently cannot be avoided, and when a pre-operative or operative obstruction cannot be overcome by an anastomosis operation at the same sitting. It is especially valuable in operation for a perforated gastric or duodenal ulcer with peritonitis, or in intestinal paresis. It removes the toxic intestinal contents from the stomach, and the distention of the upper part of the abdomen, and thereby protects, from internal pressure, the ulcer often sutured

with difficulty. Any operation necessary for an existing stenosis may be postponed until a later, more favorable, time. The gastrostomy is best performed according to the technic of Witzel. The aseptic introduction of a soft catheter will be rendered easy through a suitable canula. A purse-string suture is first introduced, including about a square centimeter of the anterior wall of the stomach. This portion of the stomach is seized on both sides by tooth forceps and held up, when it is penetrated within the suture circle by the canula armed with the soft catheter. A small incision through the serous and muscular layers makes this more easy. The canula is then withdrawn and the catheter allowed to remain. The purse-string suture is then tied, the catheter invaginated a few centimeters and held there by a chromic catgut invagination suture. Nyström does not fix the stomach to the abdominal wall, but allows it to remain completely free and the catheter to pass between the sutures of the abdominal wall, the wound in which is completely closed in the usual manner. After about two weeks the catheter is usually loose and may then be removed if all is going well.

A Review of the Literature of Fractures.—HUNTINGTON (*Ann. Surg.*, 1915, lxii, 264) from a comprehensive survey of the literature concludes that the public demands, and is entitled to, better results from fracture treatment than have, hitherto, been obtained; that from 80 to 90 per cent. of long bone fractures can be successfully treated by the closed method; that conservative treatment exacts a high degree of skill and close attention to details; that resort to the open method is of too frequent occurrence; that the least possible amount of foreign fixation material should be the rule; that steel plates, in the treatment of fractures, are a menace from the standpoint of permanency; that the bone implant is the fixation material of choice; that intramedullary splints are inferior to the autogenous bone implant; that fixation material of whatever type is not to be relied upon for maintenance of alignment; that cases of non-union and faulty union which come to secondary operation indicate indifferent methods of primary treatment; that operative treatment of compound fractures should be withheld until the external wound healing is perfected; that many joint fractures can only be treated successfully by the open method; and that normal contour and good function are closely related in end-results of all fractures.

Banti's Disease.—KRULL (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1915, xxviii, 718) says that the so-called Banti's disease is an unusual form of the so-called atrophic cirrhosis of Laennec. This deviation consists in the unusual size of the splenic enlargement and in the clinically more or less strong protuberance. The frequent occurrence of vomiting of blood accounts for the high-grade anemia. As in liver cirrhosis, it is often impossible to discover a cause. At times, however, a preceding condition can be held accountable, as syphilis, congenital or acquired, malaria or gastric disturbances. The weight of the spleen as given by Banti (1000 to 1500 gm.) is much too low. It is better not to fix the weight definitely, since it has been repeatedly shown that the splenic swelling is not proportionate to the weight. A so-called Banti's spleen is described as follows: The normal shape is preserved, the capsule is

thickened, the consistency increased, and the parenchyma is usually of a dark red color, but sometimes is brighter red. The pulp and Malpighian corpuscles are the seat of a more or less advanced sclerosis. With regard to the anemia which all investigators, almost without exception, have established by inspection; one is surprised to find that the red blood corpuscles are not much below normal, as one is inclined to expect. Cases with 4,000,000 red blood corpuscles have been repeatedly reported. This contradiction finds its explanation, aside from the fact that inspection alone cannot be depended for the diagnosis of an enemia, in the greater reduction of the hemoglobin than of the red blood corpuscles. Leukopenia is also present in this condition. In connection with the liver, the other chief organ involved in Banti's disease, Krull says: The connective tissue is increased. The surface is rough and irregular, but the organ is not necessarily always contracted. Ascites may occur; jaundice, when present, is slight. Besides nosebleeding, which Banti mentioned, gastric hemorrhages occur repeatedly in the course of the affection.

Operative Treatment of Tumors of the Bladder.—GARDNER (*Ann. Surg.*, 1915, lxii, 456) says that the results of operation on tumors of the bladder during the past fifteen years, as presented in his paper, were gathered through the old method of sending blanks to a number of the leading urologists, asking for answers to specified questions. In this way the records of 369 cases have been procured (Watson's report of 1160 cases, including Beer's 183 cases treated by high-frequency current, Oudin, has been taken as the basis of this report). Since publishing his report and within the past five years Beer has seen 59 additional cases. Judd's report of 114 cases at the Mayo Clinic is also included, which makes the total 1702. He concludes that : In the treatment of carcinoma the transperitoneal method as used in the Mayo Clinic or the subtotal cystotectomy of Squier, with wider resection of the bladder wall, offers the best method. These methods give the operator opportunity to look for enlarged glands or metastases and if necessary the ureters can be easily transplanted. Cystotomy and excision and actual cautery should only be used in terminal cases as a palliative method to relieve pain and hemorrhage. When the growth involves both ureters Watson's operation of total cystectomy with a primary operation for transplanting the ureters into the loin shows the best results. In the treatment of papilloma, intravesical high-frequency current, during the short time it has been used, has given better results than any other method, reserving the question for time and statistics to determine whether this method by reason of the difficulty in distinguishing between papilloma and carcinoma is shown to be as satisfactory as wide resection, such as is advised for carcinoma.

Errors in Diagnosis of Renal and Ureteral Calculus.—CABOT (*Surg., Gynec. and Obstet.*, 1915, xxi, 403) says that in a recently undertaken study of 153 cases of stone in the kidney and ureter at the Massachusetts General Hospital, it was noted that 26 abdominal operations had been done upon these patients without relief of the symptoms, which were clearly due to the overlooked calculus in kidney or ureter. The appendix was the most frequent sufferer and was removed in 10 cases

without benefit. What are described as exploratory laparotomies came next in frequency, with 8 cases. Fixations of a kidney supposed to be movable and producing symptoms followed in order with 4. Then came removal of tube and ovary, unsuccessful search for gall-stones, an attempt to relieve adhesions, which did not exist, stripping of the capsule of the kidney for nephralgia, and as a crowning iniquity, suprapubic cystotomy on a normal bladder for a stone which was seated some two feet away. Cabot lays down the following rules as likely to avoid these errors if carefully followed: In all cases of abdominal pain of a chronic or recurring type, in cases of backache, lumbar or sacroiliac joint strain and lumbago, careful repeated examinations of the urine, including a microscopic examination of the sediment in all cases whether albumin is present or not, and of a catheter specimen in all female patients, should precede positive diagnosis. In most of these cases in which the symptoms warrant the consideration of operation, roentgen-ray plates are essential. The evidence presented by the roentgen-ray alone is insufficient to warrant operation in most cases of stone in the kidney or ureter. Possibility of error by mistaking other foreign bodies should be excluded by the use of the ureter catheter, stereoscopic plates, injected roentgenograph, or the waxed tip catheter. In any case in which the symptoms suggest ureteral calculus and a doubtful shadow appears in the roentgen-ray plate, if the ureter cannot be catheterized on repeated attempts or the catheter is arrested at the same point on various occasions, the decision for or against operation must be made upon the apparent gravity of the symptoms. In cases with symptoms suggesting stone in the kidney, with a normal urine, a negative roentgen-ray, and an unobstructed ureter, the wax-tipped catheter will not infrequently lead to a correct diagnosis and will be likely to fail only in the cases in which the stone lies in a dilated calix and is therefore out of reach of the catheter.

Shock and Hemorrhage: An Experimental Study.—Mann (*Surg., Gynec. and Obstet.*, 1915, xxi, 430) says that the problem at hand was to determine whether there is in shock an actual loss of circulating blood and, if so, whether the loss can be accounted for by vasomotor failure. The amount of blood that can be obtained from a large arterial trunk—as the femoral—is the measure of efficient blood; it is the amount which can be returned to the heart and lungs and, after aeration, be pumped out to feed the tissues. The blood which can be secured from the venous side of the circulatory system—as from the right auricle—is the amount that is freely movable but was not returned to the arterial system. Their sum is the amount of mobile blood in the body. This sum subtracted from the total amount of blood gives the quantity of immobilized blood; the fixed quantity in the tissues. So far as the immediate circulatory needs of the organism are concerned, this latter amount of blood is useless. He summarizes his experiments as follows: In a normal dog 66 per cent. of the blood can be obtained from the femoral artery and 10 per cent. from the heart, making a total of 76 per cent. which can be secured, leaving 24 per cent. in the tissues. In an animal in which the cervical cord is sectioned, producing medullary vasomotor paralysis, 54 per cent. of the blood can be obtained from the femoral artery and 12 per cent. from the heart, a total of 66 per cent.,

leaving 34 per cent. in the tissues, In an animal in which blood-pressure is depressed practically to zero by an overdose of ether, 46 per cent. of the blood can be obtained from the femoral artery and 13 per cent. from the heart, making a total of 59 per cent., leaving 41 per cent. in the tissues. In an animal in which the viscera have been exposed until the clinical signs of shock are present but in which the vasomotor reflexes are as active or even more so than in the normal condition, only 28 per cent. of the blood can be obtained from the femoral artery and 11 per cent. from the heart, making a total of 39 per cent., leaving 61 per cent. in the tissues. He concludes that: The clinical signs of shock which appear after section of the abdomen and exposure of the viscera are due to a loss of circulatory fluid. This loss of fluid is not dependent upon any primary impairment of the medullary vasomotor centre and takes place at a point beyond the control of the vasomotor mechanism. The causes for this loss of fluid are apparently the same as those which determine the accumulation of fluid in any irritated area and produce the signs of inflammation. The nervous system probably plays no greater part in the former case than in the latter. The condition is made grave when the viscera are exposed because of the great vascularity of the tissues involved.

A Radical Operation for Hemorrhoids by a Simple Suture.—TILLMANN (*Zentralbl. f. Chir.*, 1915, xlii, 737) describes his operation as follows: According to the size, character (pedunculated or not) and number of the hemorrhoids, the local anesthesia will be produced either by a simple injection under the nodes or by a circular injection of the anus. Deep analgesia of the internal and external sphincters by the latter method will be necessary for the stretching of the sphincter and will require a 1 per cent. novocain in solution. For the more superficial injection a 0.5 per cent. solution will be sufficient. Each hemorrhoid is pulled outward by a forceps and then grasped in a radiating direction by a suitable clamp. A catgut suture is used to complete the operation. The needle is passed through the pile at the anal end of the clamp and under it. It is tied and the free end left long. Then it is continued to the other end of the pile as a continuous mattress suture. This portion of the suture serves as a protection against hemorrhage and at this point it is permitted to hang aside unknotted. Now the pile is cut away close to the clamp and the clamp removed. The suture is again used to bring the wound edges into close apposition, and when this is completed the two free ends will be together again at the anal end of the pile where they are tied together. The separate nodules or piles are treated in the same way. The special advantages of the operation are; its bloodlessness, the exact union of the wound edges, and therefore the diminished risk of infection, the rapidity with which the operation can be completed and its simplicity. In the first year of the war 40 cases were thus treated. The average time after operation before the soldier was ready for service was 14.7 days.

Eckehorn's Operation for Prolapsus Ani in Adults.—BECKER (*Zentralbl. f. Chir.*, 1915, xlii, 772) says that prolapse occurs in war time, usually from long-continued diarrhea, and may be so troublesome that the soldier is unfit for service. In 1 case the prolapse was 3 cm.

long, bled freely, was ulcerated and difficult to reduce because of the welling, and recurred after every defecation. Under local anesthesia on both sides of the coccyx, a long pedicle needle is introduced first on one side of the coccyx. Two fingers in the anus hold up the prolapse. Under the guidance of the finger the needle is pushed on under the mucous membrane to a point opposite its entrance and made to emerge at the junction of the skin and mucous membrane. The end of the suture is then held and the needle withdrawn. On the other side of the coccyx, the needle not armed with the suture is again introduced in the same manner as before and made to emerge again at the same point near the junction of the skin and mucous membrane. The free end of the suture is threaded into the needle and both withdrawn through the last needle canal. While two fingers hold back the prolapse, the two free ends of the suture coming out on the two sides of the coccyx are tied together over a tampon. Moderate diet is given for three days, and 20 drops of tincture of opium 3 times daily. The first stool should occur five days after the operation. The suture remains twenty days, and during that time is frequently tightened over a new tampon. There has been no recurrence of the prolapse after three-quarters of a year.

Gastric Fistula with Suction Drainage for Atonic Conditions of the Stomach and Intestine.—Gross (*Zentralbl. f. Chir.*, 1915, xlii, 785) refers to Nyström's recent article on gastrostomy for stomach drainage (abstracted Progress of Surgery, page 285). He has had an experience with over 200 cases, and during 1913 and 1914 made a special study of 47 cases. Since then he has used the suction drainage in 33 new cases and has established its great value. It guarantees in atonic conditions of the stomach and intestines, a continuous evacuation of the retarded contents and permits at the same time an immediate introduction of suitable quantities of fluids from the mouth. On the basis of his material, Gross considers it an important aid to operation in (1) peritonitis, even in the beginning when there is only threatened atony; (2) ileus, as soon as frequent vomiting sets in and distention of the stomach occurs or is anticipated; (3) acute dilatation of the stomach; (4) infections or other affections of the upper and middle abdominal regions which cause a gastric disturbance or make its early occurrence probable; (5) perforation of a gastric or duodenal ulcer, after the perforation has been attended to. He employs the old method of performing simple gastrostomy. A small area of the stomach surface is attached to the abdominal wall by a few sutures and is opened between two forceps, wide enough to permit the introduction of a firm rubber tube 5 to 8 cm. into the stomach. A glass tube union between this and another longer rubber tube passing into a vessel on the floor, provides for control of the current by the eyes and for suction drainage. Gross objects to the use of so small a tube as a No. 14 to 18 Nélaton catheter. With the associated complete paralysis of the intestines and the antiperistaltic stream which keeps the pylorus open, he thinks it impossible for so small a tube to carry off the fecal masses that are present. In other respects he regards Nyström's contribution as a very valuable one, since it promotes the idea of the necessity for the continued evacuation of the stomach in atony of the stomach and intestines.

THERAPEUTICS

UNDER THE CHARGE OF

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Is There a Successful Treatment of Scarlet Fever.—Koch (*Deutsch. med. Wchnschr.*, 1915, xli, 372) says that during a period of ten years the mortality of 1438 cases of scarlet fever treated by Barasch on the ordinary plans of treatment was 15 per cent. He compares this with his own mortality of 1.1 per cent. in 263 cases and ascribes the discrepancy entirely to his systematic use of serum therapy. The course of scarlet fever during the period embodied in this report of Koch's was not milder that usual, rather the reverse, for a larger proportion than normal were of a more severe type. Koch advocates strongly the intravenous injection of large quantities, at least 100 c.c., of serum taken from patients convalescent from scarlet fever. In the statistics of Barasch, Koch points out as noteworthy the fact that the majority of the patients died during the early stages of the disease and the minority died later from various complications. This is an important point for it is during the early stages in particular that serotherapy is most efficacious. Koch regards it as almost specific during this stage and says that the prompt effects seen in this connection far surpass those of autotoxin in diphtheria. Normal serum also is of distinct therapeutic value but the serum of convalescent patients is more powerful. It is also of distinct advantage to use the mixed serum obtained from several convalescent patients. He warns against the subcutaneous method of giving the serum, and inadequate dosage. The serum should be sterilized before injection and it can be kept in ampoules after sterilization and the addition of 0.5 per cent. of a 4 per cent. solution of phenol. The dose should be at least 50 c.c. for young children and 100 c.c. for older ones.

Intravenous Iodid Therapy.—Klemperer (*Therap. d. Gegenw.*, 1915, lvi, 85) writes concerning the intravenous use of sodium iodid. The author has given over one hundred such injections and has never had any untoward results from its use. He advocates the intravenous use of sodium iodid in doses of from 5 to 20 grams, two or three times a week, especially for the treatment of syphilis where a marked iodid action is desired in as short a time as possible. Among the syphilitic affections especially benefited by such intravenous iodid medication, he mentions syphilis of the central nervous system, tabes, syphilis of the circulatory system and of the liver. Klemperer recommends this treatment particularly for syphilitic aortitis to be used in combination with salvarsan therapy. His practice is to give a small dose of salvarsan from 0.1 to 0.2 grams followed immediately by the intravenous administration of from 5 to 10 grams of sodium iodid in a 10

per cent. solution. The intraveuous use of sodium iodid, however, should not be confined to the treatment of syphilis but is recommended for any condition where an iodid medication is not well borne by mouth. Klemperer has never seen any serious untoward effects from intravenous iodid medication even in doses as high as 40 or 50 grams. Occasionally some of the minor symptoms of iodism develop such as conjunctivitis and a slight but transient headache. He has seen cases where iodid medication by mouth was not tolerated but well borne when given intravenously. The injections are absolutely painless and technically easy to perform. Examination of the urine has shown that the iodid is not excreted as rapidly when given intravenously as when given by mouth.

Report on the Allen Treatment of Diabetes.—HILL and SHERRICK (*Boston Med. and Surg. Jour.*, 1915, clxxii, 696) report a very successful series of cases of diabetes treated by the method advocated by Allen. They found that this treatment is simple, safe and very efficacious in rendering and keeping a patient sugar-free, in a much shorter time than was possible by the old method. Their method of treatment was as follows: As soon as the patient enters the ward he is put on house diet without extra bread or potatoes and kept on this for two days to determine his tolerance for ordinary diet and the severity of the diabetes. On the third day he is put to bed and given nothing but black coffee with one ounce of whiskey every two hours from 7 A.M. to 7 P.M., seven ounces of whiskey in all, representing about 800 calories. If there is much acidosis, as indicated by the amount of diacetic acid and acetone in the urine, sodium bicarbonate is given, otherwise not. The patient is kept on this regime until he is sugar-free; in most of the cases it took either two and a half or three days to accomplish this. The loss of weight is very slight; the relief of symptoms, such as pruritus polydipsia, etc., is very striking and they have never seen any indication of acid poisoning in the cases treated by this method. As soon as the patient is sugar-free, he is given "a vegetable-day," *i. e.*, vegetables containing not over 5 per cent. of carbohydrates, boiled twice, with a carbohydrate content of about 15 grams after boiling. After a single vegetable day the diet is changed to one containing a carbohydrate content of 15 grams, a protein content of 25 grams and a fat content of 150 grams. From this the diet is slowly raised, increasing first the fat, then the protein, and lastly the carbohydrate. The fat is never raised above 200 grams and the calories seldom above 2,200. On this the patients hold their weight, feel well and usually remain sugar-free. The series of cases reported by the authors is small and details of the cases are included in the article. In no case did they have any unfortunate results—never any sign of coma. In every case the patient has become sugar-free and has stayed so, on a reasonable diet which enabled him to hold his weight. Some of the cases treated were severe cases of diabetes, young people, whom they had treated before by the old method and could not get sugar-free.

Clinical Studies in Caffein.—TAYLOR (*Arch. Int. Med.*, 1914, xiv, 769) reports his observations that were undertaken to test the effect of caffein on the pathological circulatory system of the human being.

He says that results obtained experimentally by intravenous injection of caffein in animals are in no way comparable with results when the drug is given to human beings by mouth, in the usual clinical way, where the absorption is more or less delayed and in cases in which the cardiovascular system is not intact. These observations were made on fifteen patients suffering from advanced myocardial disease. Every case showed some sign of broken compensation at the time of the experiment and thirteen gave evidence of retained body fluid. Dyspnea was present in 14 cases; edema of the extremities in 13 cases; ascites in 10 cases; hydropericardium and hydrothorax, single or double, in 6 cases; tender pulsating liver in 6 cases. Other common symptoms were cough, frontal headache, weakness, dizziness, and substernal pain. All patients were reported in bed on a constant diet. Taylor notes in detail the effects observed upon the pulse rate, respiratory rate, blood-pressure, diuresis, and body weight. He sums up the clinical efficiency of caffein saying that the results were excellent in eight cases. Moderate in four, and no favorable effect was obtained in three. In one of the cases in which there was no result the vomiting and loss of sleep even on small doses more than balanced any possible good that the drug could have done. All the cases with limited results showed the nervous signs, so the absorption of the drug was assured. Unpleasant symptoms, mainly nervous and gastric, occurred in thirteen of the fifteen patients. The doses used were full doses but when they were reduced below the point where they gave nervous phenomena their cardiac value had disappeared. In five of these cases a second admission to the hospital on a return of symptoms while they were still in the institution made it possible to try the comparative therapy of theobromin sodium salicylate under the same conditions and on the same heart on which the caffein action had been tested. Its action on the urinary outflow is more prompt than that of caffein and the diuresis is larger. One can usually tell in twenty-four hours, in a given case, whether theobromin sodium salicylate will act or not; while with caffein the third or fourth day is more apt to show results. The theobromin sodium salicylate action is equally well sustained and usually at a higher level than the caffein. Where caffein has a depressing effect on the vasomotor system and lowers the blood-pressure, theobromin sodium salicylate first elevates the pressure and then later lowers it. Taylor regards 80 grains a day as a normal clinical dose. Patients will tolerate this dose easily. Not only was the theobromin sodium salicylate action prompter, much stronger and equally well sustained but it also did not show the gastric and nerve disturbances attendant on caffein. Taylor in his summary says that in myocardial insufficiency with retained body fluid, caffein causes a moderate increase in the urine output with a proportional loss of body weight. This increase reaches its maximum on the fourth day; a drop in both the systolic and diastolic blood-pressure which may stand in a causal relation to the diruetic coefficient, contrary to the usual teaching; a slight (3.6 per cent.) temporary rise in the pulse-rate, but no permanent change in either the pulse or respiratory rate; a moderate relief of the cardiac symptoms; the constant appearance of distressing nervous and gastric symptoms. He believes that the clinical diuretic action of caffein may be better performed by large doses of theobromin sodium salicylate without the unpleasant side effects.

Emetin Hydrochloride.—Robinson (*Practitioner*, 1915, xcv, 544) has had very good results with the use of emetin hydrochloride for the treatment of pulmonary hemorrhage occurring in pulmonary tuberculosis. In mild cases, he gives a dose of two-thirds of a grain daily and continues its use for five days after the sputum has become free of blood. He has found that emetin hydrochloride has been uniformly successful in checking the hemorrhage in about three days. Similar results were obtained in controlling hemorrhage from gastric ulcer by Robinson. He cites a severe case of mucous colitis associated with dysmenorrhea, who was much benefited by emetin hydrochloride and hopes that others may be led to try the same treatment for similar conditions. Robinson has found that the sole drawback to the use of emetin hydrochloride is that there is a certain amount of local tenderness after subcutaneous or intramuscular injections. This, however, is not sufficient to prevent its daily administration for long periods.

Specific Treatment in Typhoid Fever.—Gay (*Jour. Lab. and Clin. Med.*, 1915, i, 13) summarizes the history of the specific treatment of typhoid fever. The first twenty years experience since 1893 with the use of ordinary preparation of typhoid vaccines administered subcutaneously gave some encouragement for the method in the matter of symptomatic improvement, shortening of the duration of the disease, decrease of the mortality, lessening of relapses and complications, with a few abortive cures. The results obtained were of doutbful value and inspired little confidence that the true specific treatment had been found. Modern investigations have introduced the intravenous administration of dead or living cultures and particularly of sensitized cultures of the typhoid bacillus. With such methods far more striking results have been realized. Abortive cures occur in a considerable percentage of cases, perhaps in as high as 30 to 40 per cent. If one working hypothesis is correct, these abortive cures are due to the presence of antibodies in a patient who is actively combating the disease, and cure is affected by the action of these antibodies on the circulating bacteria, combined with a specific hyperleucocytosis produced by the vaccine, particularly when it is specific and sensitized. The remaining cases might possibly be favorably affected by a combination treatment of sensitized vaccine and a suitable immune serum which would supply the lacking antibodies.

Concerning Exercise in the Treatment of Severe Diabetes.—Allen (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 743) says that tests were made first in diabetic dogs, with a known constant limit of tolerance for carbohydrate or protein. It was found vigorous exercise markedly raised the tolerance of such animals, as judged by the sugar in both urie and blood. In some experiments, dogs which for months past had regularly shown glycosuria whenever they were given 100 grams of bread, on exercise were able to take 200 grams of bread as a regular daily ration without glycosuria. The tests with patients are more recent, but the results thus far appear sufficiently favorable to warrant recommending exercise as an addition to the treatment of diabetes. Some of the severest cases are too weak for exercise at first, but it is begun as early in the period of dieting as practicable and generally

the weak patient is able to do more than he or his physician supposed. In suitable cases the blood-sugar may be found to fall rapidly during a half hour or hour of lively exercise. In the earlier or more severe cases, it may rise thereafter; but often it will continue to fall after the exercise has ended, and remain for sometime at a lower level. In a patient free from glycosuria with persistent hyperglycemia, one fast day with exercise may reduce the blood sugar so much as several fast days without exercise. Allen says that it is hoped that this addition to the treatment of severe diabetes will prove of special value to children, to patients with persistently low tolerance, and perhaps to some of that class previously so hopeless, namely, tuberculous diabetics. For the ordinary type of patients it may be a means of getting results somewhat more quickly and thoroughly, and leading to a higher degree of both comfort and usefulness. The value of exercise is strictly limited. It cannot raise tolerance very high, and it is not equal to the dietary regime in importance. Results will be unfortunate if it is used merely as a means for shortening the hospital care of the patient or for building up weight and strength at the cost of more important considerations. The radical and permanent control of the diabetes is the essential matter, and is to be judged by such things as glycosuria, acidosis, and blood sugar, not by a temporary sense of well-being. A stern program of fasting, low diet, and reduction of weight is still necessary as before, but it is hoped that results may be more beneficial with the use of exercise as an additional detail of the treatment.

Poisoning by Mercuric Chlorid and its Treatment.—LAMBERT and PATTERSON (*Arch. Int. Med.*, 1915, xvi, 865) report very good results with the following treatment for acute mercuric chlorid poisoning: The first indication is to give the patient the whites of several eggs and then to wash out the stomach thoroughly. This has usually been done before the patients are admitted to the hospital. On admission, the stomach contents are expressed and examined for mercury, the stomach is thoroughly washed, and a pint of milk introduced. If no stomach contents are obtained before lavage, then the lavage water is examined for mercury. Urine passed spontaneously, or that obtained by catheter, is examined for mercury. The metal appears in the urine in from three to twenty-four hours after it has been swallowed. If more than a day has elapsed since the poisoning occurred, a stool should also be examined for the poison. If the first lavage does not allay the nausea and vomiting, it is repeated after an hour, and the following routine is begun as soon as the stomach will permit: (1) The patient is given every other hour 8 ounces of the following mixture: potassium bitartrate, 1 dram; sugar, 1 dram; lactose, one-half ounce; lemon juice, 1 ounce; boiled water, 16 ounces. Eight ounces of milk are administered every alternate hour. (2) The drop method of rectal irrigation with a solution of potassium acetate, a dram to a pint, is given continuously. The amounts of urine secreted under this treatment are very large. (3) The stomach is washed out twice daily. (4) The colon is irrigated twice daily, in order to wash out whatever poison has been eliminated in that way. (5) The patient is given a daily sweat in a hot pack. The authors emphasize the necessity of keeping up the treatment with the colonic drip enteroclysis day and

night without interruption. In cases in which one single dose has been taken, after two negative examinations of the urine, on successive days, it seems legitimate to stop the treatment. For the less severe cases, a week may be a sufficient time for treatment. When large or successive doses have been taken, or when there is a preëxisting kidney lesion, or when treatment begins several days after the poison is taken, longer periods of treatment, up to three weeks, are necessary. Under the treatment detailed above, these patients quiet down to their routine and, as a rule, do not suffer except from the discomforts of the therapeutic measures. The stomach becomes tolerant of the milk diet and the alkaline drink after from twenty-four to thirty-six hours. The kidney secretion at first is excessive, and may run up to 130 or more ounces in the twenty-four hours. This usually diminishes in spite of the continued exhibition of fluid between the fifth to the tenth day, and may nearly stop altogether. It is at this period that the continuous water cure and the rest in bed must be insisted on. If this period is successfully passed, the secretion of urine again increases often to a higher level than at first. The mercury itself seems to act as a diuretic at this stage of the treatment. The bowels usually show some irritation, but when the treatment is faithfully carried out, the tendency to diarrhea and colitis is regularly controlled by the colonic irrigations, and other medication for this symptom has been rarely necessary.

Coagulen in the Treatment of Pulmonary Hemorrhage.—Riedl (*Wien. klin. Wchnschr.*, 1915, xxviii, 7) advises the use of coagulen to control pulmonary hemorrhage. Coagulen is prepared from the blood platelets of animals. It is a yellow powder, soluble in water and its solutions can be sterilized without destroying its efficacy. The theory of its action is that the blood platelets are supposed to contain the thrombozyme which unites with the thrombogen of the blood plasma and, in the presence of calcium salts, causing clotting of the blood. Coagulen has been used as a local hemostatic in operations and Riedl advocates its use hypodermically and intravenously in internal bleeding. He believes it is effectual to control bleeding in hemophilia and other hemorrhagic diathesis. When used intravenously solutions in the proportion of 1 gram of coagulen to 10 c.c. of distilled water are used after sterilization by boiling for a few minutes. Reidl has had success in the treatment of pulmonary hemorrhages with such injections and advocates the more general use of this remedy for that purpose.

A Study of Different Nitrogenous Diets in Chronic Nephritis.—Frothingham and Smillie (*Arch. Int. Med.*, 1915, xv, 204) believe that it is justifiable to conclude from their study that in certain types of chronic nephritis the nitrogenous content of the diet should be carefully watched in order to prevent an increase in non-protein nitrogen in the blood. The exact effect of an increase in blood nitrogen produced by a high nitrogenous diet is not known at present, but presumably it is unfavorable to the best interests of the patient, since in some it increases their discomfort. A diet low in nitrogen content will frequently keep down to normal the non-protein nitrogen of the blood in chronic nephritis.

PEDIATRICS

UNDER THE CHARGE OF

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Treatment of Infantile Beriberi.—JOSÉ ALBERT (*China Med. Jour.*, 1915, xxix, 381), in an interesting article on infantile beriberi, holds this to be the most interesting problem of pediatrics and of general medicine in the Philippine Islands. It is without parallel elsewhere, since the infant mortality among breast-fed children is greater than that among the artificially fed. Among children under one year 38 per cent. are victims of the disease. Hirota, of Japan, has established that infantile beriberi is a true intoxication from ingesting beriberic milk, and that the discontinuance of maternal feeding is the only and safe means of cure which occurs during the first week of the procedure. The substitution of artificial feeding being extremely difficult and usually dangerous among the class of people affected. Bréaudat, Gabriel and Guerrero fed the mothers of beriberic infants with rice polishings (tiqui-tiqui) and mango—two antiberiberic foodstuffs. Owing to the unpalatability of this food and the necessity of employing artificial feeding for a certain length of time, the method did not spread. Chamberlain and Vedder of the U. S. Army Board advocated the use of the extract of tiqui-tiqui without the discontinuance of maternal feeding. Five cubic centimeters of the extract represent 82 grams of rice polishings. The dose is 5 c.c. a day given in 20-drop doses every two hours while the child is awake. The use of this extract, if given in time and in sufficient doses, is followed by immediate and marked improvement, the clinical syndromes change in twenty-four hours, and in three days the disease has disappeared with the exception of the aphonia, which lasts for seven or eight weeks. Treatment should be continued as long as aphonia persists. In stubborn cases the dose should be increased. In cases without aphonia treatment should be continued at least three weeks after apparent cure. Failure of the extract to effect a cure may be due to extreme severity or advanced neuritis, cases associated with other infections such as bronchopneumonia, and deficiency of the active principle in the extract. The extract is a vagotropic drug, supplying vitamines to the vagus nerve.

Serum Treatment of Scarlet Fever.—EMIL REISS and JOHANNA HERTZ (*München. med. Wchnschr.*, 1915, lxii, 1177) report further observations on the treatment of scarlet fever with convalescent serum. They have come to the use of this form of treatment almost routinely instead of using it only in the most toxic cases with poor prognosis. In one year 33 children were treated by the serum method out of 413 cases of scarlet fever admitted. The 33 cases included only acute, toxic cases with doubtful or poor prognosis. Of this number

but 1 died of the fulminating type of fever and 2 others died from subsequent intercurrent conditions. Most of the treatments were given during the first five days of the disease. Convalescent serum was used in this series, and the most significant factor in the result was the marked improvement in the general condition. Cyanosis disappeared, breathing became quieter, the pulse slowed and became stronger and delirium and stupor cleared up rapidly. These changes usually occurred within four to twelve hours following the treatment. Whenever the convalescent serum was given early enough and in sufficient dose (50 c.c. to 100 c.c.) the effect on the temperature curve was marked. A slight rise of 0.2° to 0.5° occurred within a half- to one hour, followed in from one to four hours by a marked fall of from two to three degrees. Any subsequent rise to the original height was always caused by some complication. Usually the fever fell to normal by a swift lysis. Small doses of 25 c.c. may often be sufficient, but larger doses are more surely active in the long run. The intravenous method was almost exclusively used. Four cases were treated with normal serum or a mixture of normal and convalescent serum. While the general improvement occurred, it was much slower and less marked and in 1 case the temperature alone was affected and the general condition remained the same. The authors report the recovery of the most severe case they have ever seen, by repeated injections of the convalescent serum. The child recovered with evidence of degenerative changes in the central nervous system, probably due to the severity of the infection which the serum was not quite sufficient to counteract. A *résumé* of their technic follows the article.

Influenza Meningitis.—Alan Brown (*Canadian Med. Assoc. Jour.*, 1915, v, 1076) reports 2 cases of influenza meningitis in children, emphasizing that the influenza bacillus is a not infrequent cause of meningitis. The most prominent and invariable characteristic of this bacillus is its hemophilic property, and next to this its pleomorphism. It may be considered as conclusive that a pseudo-influenza bacillus does not exist. This bacillus is capable of causing inflammation of the serous membranes anywhere in the body. The upper respiratory tract appears to be the most frequent portal of entry into the body. In the cases reported the meningitis developed during an attack of clinical influenza. In 1 case blood culture during life showed a pure growth of influenza, as did also cultures from the brain, heart's blood, left lung and mastoid taken postmortem. The only effect of influenzal serum injected intraspinally was an increase in plagocytosis. In this case the path of infection was apparently through the ethmoidal plate with practically no involvement of the lungs. The character of the spinal fluid in this condition is fairly uniform, being cloudy, depositing a whitish-yellow sediment and becoming more purulent as the disease progresses. Polymorphonuclears are increased. The morphology of the bacilli vary greatly. Lumbar puncture gives early and correct differential diagnosis in this disease. It is doubtful whether the bacilli are ever present in a clear spinal fluid. There have been slightly over 50 cases of pure influenzal meningitis reported since 1899. Six are reported to have recovered, 1 following the use of influenzal serum.

Prophylaxis in Pediatrics; Institutional.—CARROLL (*Pediatrics*, 1915, xxvii, 439) criticises the plan still in use in many hospitals of keeping in one general ward all classes of cases, surgical, skin, neurologic, orthopedic, etc., mingled with general medical and feeding cases and convalescents roaming almost at will and playing with the much-handled and not innocuous ward toys. The two points in common in all these cases are that all are of a pediatric nature as far as age is concerned, and that their physical resistance to disease has been lessened. The problem presented by this condition of affairs is: Lessened physical resistance plus bacteria, plus a means of transmission, plus proximity equals what? The chance of cross-infection is good. The mortality tables of the ward register tell a very pointed tale. Many patients with fair prospects lose all they have gained at the onset of an unsuspected cross-infection and only two frequently succumb either to the primary or secondary infection. The specific causes of this cross-infection include the diseases of mumps, measles, pertussis and scarlet fever, which have no proven specific factor but which comprise three-fourths of the usual sources of infection in institutional wards. The surgical cases contribute the streptococci and staphylococci, the orthopedic, the tubercle bacillus, the specialties, gonococci and streptococci and the medical types a galaxy of all kinds. The means of transmission comprise the ward furnishings, the hands of the professional attendants, and the toys. Under such conditions even with the best of intentions what can be done in the way of prophylaxis? A greater degree of prophylaxis is secured by the ideal system of a ward composed of units each containing between five and eight patients. Each unit is independent, patients can be grouped under any chosen system, and when infection occurs units can be isolated and the entire health of the ward has not been exposed. When the general ward cannot be dispensed with, medical cleanliness by sterilization of every article used on different patients and of the hands of the attendants will reduce the chance of infection proportionately to the degree to which it can be observed.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Abortion Complicated by Fever.—BENTHIN (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 2,) refers to his previous publications and the value of expectant treatment in cases of abortion complicated by fever. He then reported a morbidity of 29 per cent. and a mortality of 9.8 per cent. by active interference, and a morbidity of 9.8 per cent. and a mortality of 0.9 per cent. by conservative treatment. In the presence of the dangers from hemolytic

streptococci, interference is especially dangerous, for in the cases treated by active interference the mortality was 31.2 per cent., whereas by conservative treatment the mortality was nothing. In 23 cases where hemolytic streptococci were present in the uterine cavity, 20 had fever after some interference with the uterus. He quotes 5 cases treated by curetting, of whom 1 died and in each instance, the temperature rose markedly after the exploration of the uterus. His experience shows a mortality in those cases having hemolytic streptococci, treated by active interference, of 18 per cent. In a series of 19 irrespective of the variety of germs present, treated by exploration and evacuation of the uterus by curette and finger, the mortality was 73 per cent. The writer collects a considerable number of statistics which need not be quoted, but which show distinctly that in abortion complicated by fever, interference with the interior of the uterus should be avoided. He described 3 cases in which the uterus was cleared out because it was suspected that placental pieces remained and in which death followed. Autopsy showed in each instance peritonitis and pyemia. If one could be sure that the streptococci present in the uterus in a case of abortion complicated by fever were not hemolytic, and there arose some occasion for interference, one need not hesitate under these circumstances to do so, with the probability of a good result, but in the presence of hemolytic streptococci, interference should not be practiced. The finger only should be employed and the curette should not be used. While there are many theoretical considerations which would urge the universal emptying of the uterus in abortion complicated by fever, the clinical results of the expectant treatment are so markedly extraordinary that certainly a thorough trial of this method is indicated.

Auto-infection.—BENTHIN from Winter's Clinic in Königsberg (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 2) discusses this question in the light of his practical experience. There are many factors alleged to militate in favor of auto-infection and they are not, as a rule, sharply defined. One of the first statements commonly made concerning this subject is that auto-infection occurs in those cases where infective bacteria were not artificially placed within the body. This, however, does not explain all cases, as it is not possible to give the origin of infective germs found in the vagina, and yet their presence during pregnancy is undoubted. While it is often asserted that bacteria introduced within the vagina in pregnancy soon disappear, on the other hand, Benthin has used vaginal injections of 5 per cent. lactic acid for weeks and has found hemolytic streptococci at the end of the time. As regards the diagnosis of such a condition, Winter relies primarily upon bacteriological examination. A clearly drawn distinction must be made between endogenous and exogenous infection, and one must recognize also clearly the presence or absence of pathogenic bacteria. Cases where there is no doubt that pathogenic bacteria were present in the region of or near the infected area before the beginning of the disease must be considered as auto-infection. Where one cannot prove in this way that bacteria were present before the outbreak of infection, the cases must be classified as those infected without. It is not sufficient to isolate bacteria, but control cultures are required. This doctrine raises the question, naturally, of the meaning of Aschoff's theory of auto-infection. The presence of pathogenic bacteria in the

secretions of healthy persons, the varying import in prognosis with such persons, the frequency of infection with bacteria produced in the body itself, are all questions which stand or fall with the doctrine of auto-infection. Clinically, bacteriological examination has shown that pathogenic bacteria which develop late in the puerperal period as the cause of septic infection were frequently present before labor. The sort of bacteria is of importance, as the hemolytic streptococci are obviously the most virulent. The prognosis in a given case may often depend upon the presence or absence of repeated examinations and trauma sustained during operation. The reports of the Frankfort Clinic, showing that the presence of the hemolytic streptococci had no especial influence on puerperal morbidity and mortality are not borne out by others. In a series of obstetric operation upon patients in whom hemolytic streptococci were present before the operation, 33 per cent. developed puerperal infection, while in cases in which the hemolytic streptococci were not present, but 14 per cent. developed puerperal sepsis. It is obvious that in those cases where there is reason to suspect the presence of streptococci before labor, that the best results will be obtained as in the Frankfort Clinic, when examinations are made by the rectum only and when vaginal examinations and explorations are conducted as rarely as possible. We must, however, recognize the series of cases of auto-infection in which bacteria make their way upward from the vagina into the tissues of the uterus. In gynecological cases the spontaneous ascent of bacteria is comparatively rare and unimportant. Endometritis may be present but whether lesions in the parametra result in this manner cannot well be known. Where, however, operations are undertaken, auto-infection is a frequent cause of septic disease. Where before operation hemolytic streptococci are present in great number, the prognosis is especially bad. It is interesting to observe that infective bacteria may be present in pregnant women in the mucous membrane of other than the generative organs. Thus we frequently find them in patients who have recovered from some definite infection and usually saprophytic germs are those present. The nasal mucous membrane is a frequent home for infective bacteria. Thus in 111 cases examined, Haslauer found but 8 free from bacteria. The staphylococci are most often there; also the pneumococcus. Streptococci are sometimes found and in Haslauer's 111 cases, in nasal cavities supposed to be normal, streptococci were present in 32; diplococci in 37; staphylococci in 47, diphtheria bacilli in 24. In 57 cases in which the nasal mucous membrane was apparently normal, Besser found streptococci seven times and yet recovery after operations upon the nose is usually undisturbed by septic infection. Where however, streptococci are present, such may not be the case. Thus 7 out of 10 of these cases had fever and infection after operation. After the removal of adenoids, fever has been reported in from 38 to 50 per cent. of cases and general septic infection and not infrequently infection of the sinuses. In the mouth and about the jaws, the Streptococcus pyogenes and diphtheria bacilli have been found. In 200 cases streptococci were abundant. While in the normal nose hemolytic streptococci were not found, in the mouth and jaws they were present in 30 per cent. of cases. Others detected the Streptococcus pyogenes in from 5 to 62 per cent. of cases. Where the vessels are hypertrophied

there is usually a pure culture to be obtained. In angina hemolytic streptococci have been frequently observed. The ear records of otological societies and their papers upon the subject show that the actual chamber of the ear should be sterile, but, when once infected or inflamed, bacteria are always present, of which streptococci are the most significant. In 292 cases of otitis media Liebmann found streptococci in 189, and in 19 pneumococci. Other observers report bacteria in other portions of the ear quite frequently. In 1907 Süpfle found Streptococci pyogenes in 60 per cent. of cases of otitis media. In chronic middle-ear disease bacteria are also present. In the eye, one must remember that the conjunctival sac is well adapted to harbor infective germs. Kraupa found but 33 per cent. sterile in a considerable number. Again the streptococcus is the important germ, ranging from 23 to 43 per cent. Where streptococci only are present, their presence does not seem to militate against the success of operations, but streptococci forbid operation so long as they are present. Kraupa believes that by using oxycyanate of mercury 1 to 5000 he can secure a sterile condition of the conjunctival sac in a few days. That this preliminary treatment is valuable is shown by Elshnig and Ulbricht, who in 179 cataract operations had but 0.6 per cent. of failure through infection, while in 137 cases where no prophylactic measures were taken, and various operations were done, the morbidity was 5 per cent. The practical conclusion remains that, under some circumstances, bacteria which are present in the secretion of a mucous membrane may cause disease after some interference with this membrane, whether by surgical procedure or by parturition. It is important to recognize, if possible, the sort of bacterium which is present. The fact that fever may not be present does not positively prove the absence of danger, for some most severe infections are afebrile. It is important to know that when fever develops it is probably caused by germs which were in the vagina before labor. The reason for ascertaining the precise sort of bacterium lies naturally in the effort to produce sera or vaccines which may be of service to the patient. Benthin has no especial confidence in vaginal injections given before or during labor and believes that we cannot mechanically remove every bacterium found in the vagina. Unquestionably, septic disease would become more and more infrequent as external asepsis is carried out thoroughly, and unnecessary examinations and manipulations are avoided. It will be a very difficult thing to entirely overcome auto-infection, but the effort should certainly be made. No consideration of the subject of auto-infection in parturient women can be complete without reference to decaying teeth. The notable tendency of dental caries to increase rapidly during pregnancy naturally suggests this fact. In the reviewer's experience a primipara passed through a spontaneous normal labor under antiseptic precautions and without much injury. On the fourth and fifth days, with normal lochia and secretion of milk, her temperature rose to 102° and 103° and 104°F. No pelvic condition accounting for this could be found, and a thorough search was made of the patient's body for some focus of previous infection. The patient had been to her dentist very shortly before confinement and was pronounced in good condition. While pressing along the jaw a tender point was found, and the patient stated that some years before she had there had inflammation about

the root of a tooth. Her dentist was summoned, who incised at this point, obtaining about 2 drams of exceedingly foul pus. The emptying of this pocket was followed by the disappearance of the fever. Ultimately, so extensive was the caries, that a piece of the jaw-bone had to be excised by a surgeon to secure a sound healing.

GYNECOLOGY

UNDER THE CHARGE OF

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Treatment of Uterine Perforation—Radical or Conservative.—It is easy to lay down the dictum that perforation of the uterine wall during an attempt to evacuate retained secundines should never occur, but so long as the operation is performed, especially by those not especially trained in gynecological surgery, and often under unfavorable surroundings, there are bound to be occasional cases of perforation of the softened uterine wall by the curette or placental forceps. It is commonly believed that such injuries are rarely fatal unless accompanied by distinct evidence of injury to some abdominal viscus, and may therefore be treated by a "watchful waiting" policy; while this is undoubtedly true in certain cases, the fact has been forcibly brought out in a recent article by SCHWEITZER (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, xlii, 148) that in the majority of cases, the condition is more serious than is often believed. Schweitzer has collected from the German literature of the last five years 105 cases, reported by 49 different surgeons: notwithstanding the fact that most of these cases were brought under the care of trained gynecologists, the total mortality of the entire series was something over 25 per cent. In no less than 48 of the cases had injuries to the intestines occurred, with 18 deaths; there were 6 cases of simple intestinal prolapse, with 1 death; 10 of omental injury, with no deaths. In 2 cases the tube and ovary were injured, in 1 the bladder injured (died), and in 1 the ureter was torn loose both at the renal and vesical end (recovery after nephrectomy). In 1 case even the cartilage at the sacral promontory was torn loose. The dangers that may beset the expectant method of treatment for cases of uterine perforation are shown by the fact that of 17 cases so treated, 9 died, a mortality of over 50 per cent., much higher than that of the series as a whole, or of the cases treated by laparotomy. Of these 9 fatal cases, 6 died from peritonitis, 1 from general sepsis, 1 in collapse, 1 from cachexia following a utero-intestinal fistula. Of those that recovered, only 2 patients came through without serious complications; in three instances there were utero-intestinal fistulæ which healed, in 1 intestinal adhesions caused obstruction, for which subsequently a laparotomy had to be performed; in another, a pelvic abscess formed which required drainage,

etc. From these figures, the author draws the conclusion that the only cases which may safely be treated expectantly are those in which the perforation is evidently small, the uterus completely empty and apparently not infected, and in which no evidence of intestinal injury is present. All others, he thinks, should be subjected to immediate laparotomy. With regard to the treatment of the perforated uterus, once the abdomen is opened, Schweitzer thinks the best policy is in most cases to remove it, rather than to try to repair the injury by suture, since the latter procedure cannot prevent a secondary infection of the peritoneal cavity if the uterus is infected, a condition that it is impossible to exclude in cases of this sort. The statistics that he has been able to collect on this point, while based on rather small series of cases, bear out this contention as far they go. Of 12 cases treated by suture, 1 died (8 per cent.); of 24 cases treated by hysterectomy, 1 died (4 per cent.). With regard to the prevention of injuries of the class under discussion, the author insists that the curette should never be used in cleaning out an abortion, and placental forceps only to remove pieces of material that have been completely freed from the uterine wall by the finger. He insists that all the actual work shall be done by the finger only, and very rightly condemns utterly the practice of indiscriminately curetting or using the forceps without ever introducing the finger through the cervix to palpate the interior of the uterus. If these simple principles were more generally observed, he says, we should have practically no cases of perforation to treat.

Treatment of Pelvic Inflammation with Ultraviolet Rays.—The success obtained by the treatment of surgical tuberculosis with ultraviolet rays suggested to FROMME (*Zentralbl. f. Gynäk.*, 1915, xxxix, 598) to try the same method in chronic gynecologic inflammations. The rays are obtained from a so-called "artificial sun lamp," which is apparently of the mercury vapor type. The rays are applied directly to the abdomen, the remainder of the body being covered to prevent injury. The first application lasts, as a rule, only one and a half minutes with the lamp 75 cm. from the skin; after a couple of days a second exposure of two to two and a half minutes is given with the lamp only 60 cm. from the skin. Then on following days the exposures are increased by two or three minutes each day until an exposure of twenty minutes has been reached, the lamp being at the same time gradually brought to within 40 cm. of the skin. A marked hyperemia always occurs after the first treatment, which gradually gives places to to a brown pigmentation, practically a sun-burn. This, however, disappears after cessation of treatment. Fromme reports that he has treated by this method 25 cases of pelvic inflammation, in nearly all of which were pus tubes the size of the fist. About half of these patients are still under treatment; 9 have been discharged as cured after an average of about 15 exposures; in 2 instances no benefit was obtained. In the ones considered cured all traces of the adnexal enlargements had disappeared. All these were treated as out-patients, merely coming to the hospital for the actual treatment, their ordinary life being in no other way interfered with. In addition to the inflammatory cases, 6 of pruritis vulvæ were subjected to the treatment, with 2 definite cures, and marked improvement in the other 4, all of whom are still

under treatment. Fromme thinks, as a result of these experiences, that the ultraviolet rays may be found to have a considerable field of usefulness in gynecology.

Ovarian Transplantation.—This operation, which has been discussed a number of times in these pages in the past few years, forms the subject of a recent clinical report by CHALFANT (*Surg., Gynec. and Obst.*, 1915, xxi, 579), which is based upon 32 cases drawn from his own experience and that of Dr. Simpson, of Pittsburg. In all these cases the transplantation was autoplastic, *i. e.*, the patient's own ovarian tissue was used for the graft. The purpose of the operation is, of course, to conserve to the woman the internal secretion of the ovaries in those cases where either from infection or damaged blood supply it does not appear safe to leave the ovary in the peritoneal cavity. The technic observed by Simpson and Chalfant was as follows: "After the ovaries were removed, a portion or all of the better one was kept in normal salt solution at body temperature until the operation proper was completed. Then a small incision was made through the skin about two inches inside the interior superior spinous process of the ilium. A pocket was made in the subcutaneous tissue by spreading a hemostatic forceps, and into this pocket a section from the cortex of the ovary was inserted and the skin closed by plain catgut suture. The same technic was followed in all cases, except that in some a transplantation was made on both sides." This particular location for the graft was chosen because of accessibility, both at the time of operation and subsequently, good blood supply, and absence of danger of intraperitoneal or retroperitoneal involvement, if the graft should be already infected at time of implantation. Of the 32 patients reported upon, 13 had one ovary left in its normal position, and should therefore, it would seem, be dismissed from further consideration. In only two instances were both ovaries removed and the uterus allowed to remain; one of these started menstruating four months after the operation, and continued regularly for six months, since which time there has been no flow, with moderate menopausal symptoms. The other patient never menstruated, and had quite severe menopausal symptoms. Of the 17 patients from whom the uterus and both ovaries were taken, 5 gave evidence of apparent continued function of the graft, as shown by variations in size and increased tenderness. With regard to the presence or absence of menopausal symptoms, which forms, of course, the crux of the situation, only 17 patients are tabulated, and it is not quite clear whether any of these may belong to the first group, in which one ovary was left *in situ*. Of the 17, however, 10 per cent. had no menopausal symptoms, 41 per cent. slight, 29 per cent. moderate, and 18 per cent. severe. In order to have a basis of comparison, the authors sent out a series of letters to patients from whom both tubes and ovaries had been removed, but in whom no transplantation had been done. Tabulation of 40 replies showed that 10 per cent. of these likewise had had no menopausal symptoms, 17 per cent. slight, 20 per cent. moderate, and 52 per cent. severe. While admitting that the above series of cases are too small from which to draw any definite conclusions, the authors consider that the comparison indicates that transplantation does lessen to some extent the severity of the artificial menopause.

OTOLOGY

UNDER THE CHARGE OF

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Mastoiditis and Erysipelas.—The fact that the mastoid operation may be performed with expectation of good results in the face of an erysipelatous inflammation has been demonstrated in primary healing under this condition but the possibility of a favorable outcome under apparently subversive conditions is emphasized in two cases reported by MAHER (*Bull. d'oto-rhino-laryng.*, xvii, 6), who had made a series of observations of operative cases under coincident erysipelatous manifestation and had been surprised at the inversive effect of the apparent complication. In the first instance a woman. thirty years of age, had an acute inflammation of the right middle ear, accompanying a nasopharyngeal infection and a right maxillary sinusitis. The patient was, moreover, suffering from a puerperal infection; paracentesis of the drum-head failed to lower the temperature or to lessen the mastoid pain and tenderness, and an antrotomy was done with complete resection of the mastoid apophysis. Two days later an erysipelatous macule appeared followed by a chill and rise in temperature and this was followed by a bilateral cervical adenitis which broke down and a pleural suppuration requiring thoracentesis. To this was added a marked albuminuria, constituting a serious clinical picture. The erysipelas completed its cycle of the face, the neck, and part of the trunk, the accompanying suppuration from the mastoid being abundant, daily dressings with sterile water were continued throughout the disease; the patient was extremely weak but, with the subsidence of the erysipelas this condition ameliorated, the postaural wound rapidly closed, and in fifteen days cicatrization was complete and the patient was fairly convalescent in all respects. The second case was that of a woman, thirty-eight years of age, with an ozena, who had complained of pain in the ear and, in a sudden attack of vertigo, had fallen forward. Examination showed the mastoid to be tender over the antrum and at the apex and that there was a marked bulging of the posterior superior canal wall almost to the extent of touching the opposite wall. Under antrotomy and removal of the major portion of the outer mastoid cortex, the cavity and the antrum and aditus were found to be filled with fetid fluid and granulomata, the lateral sinus was intact as also a considerable area of exposed dura. After operation and on the morning of the following day, the temperature remained stable but, on the afternoon of that day, it suddenly rose, increasing still further on the following day coincidently with the manifestation of a severe chill and the appearance of an erysipelatous blush upon the face, which rapidly spread to the scalp and neck; the temperature continued high for three days, the patient became excitable and delirious, requiring a straight jacket, and developed an acute mania lasting nearly a

week and accompanied by marked albuminuria. During the course of the erysipelas, the dressings of sterile water and alcohol were continued daily but the wound remained fungous and areas of exposed bone suggested the possibility of later sequestræ. As the erysipelas disappeared the general condition improved and the wound became clean, healing rapidly within a few days without elimination of the expected sequestræ. In still another case of mastoid operation in a child with slow closure of the postaural wound, the appearance of an erysipelas seemed to have a stimulating effect and the wound became cicatrized in a few days.

Massage of the Tympanopharyngeal Tube.—Tubal massage, as an adjunct to the treatment of swelling of the tubal mucosa and of incident middle-ear disease has been commended by various writers advising deep manipulation of the cervical muscle, beneath the auricle, without, or in combination with, correlative movements of the buccal and pharyngeal muscles; more direct massage has also been applied directly to the lateral pharyngeal walls by means of sounds or by the introduction of the finger covered with a rubber cot. The massage through the external muscles is comparatively ineffective because of the resistance offered and because of the impact of the pressure along the long axis of the tube and a minimum of influence exertable upon the tubal mucosa; the more direct massage through the mouth possesses decided advantages, but is open to the objection, in a large number of cases, of a maximum of discomfort from the necessary manipulation of the soft palate and the lower, and reflexly sensitive, lateral pharyngeal walls. P. J. Mink (*Ztschr. f. Ohrenh.*, 1915, lxxii, 3) therefore utilizes for massage purposes the pharyngeal applicator devised by him in 1906, consisting of a silver or white-metal rod 20 cm. in length and 1 mm. in diameter, contoured like a nasal catheter, slightly curved, to rock over the nasal septum, and bent sharply upon itself at the outer end in such a manner as to make it a tactile as well as a visual index of the direction of the tip of the sound which, wound with cotton and dipped in glycerine, is introduced, after the fashion of a nasal catheter, carried as far back as the posterior pharyngeal wall, then turned outward into the post-tubal fossa, and forward over the tubercle into the mouth of the tube, the whole tubal region being by this means easily manipulable.

Mastisol.—Theimer (*Ztschr. f. Ohrenh.*, 1915, lxxii) commends the use of a mastic solution in the preparation for surgical operations upon the ear upon the ground of personal experience in its use as an adjunct to other measures for sterilization of the operative field. That the customary methods of sterilization, following shaving of the side of the head, consisting in washing with soap and water by means of a stiff brush, with ether and with benzine are ineffectual has, in the opinion of the author, been sufficiently proved, while the disinfection of the skin by painting with tincture of iodine is open to certain objections, although the attained asepsis is complete, but in many cases the application is not well borne by the skin, which becomes irritated and eczematous and the sutured or clamped edges of the incision swollen and less well apposed. The value of the solution of mastic in benzol lies mainly in

the fact of its rapid fixation and virtual arrest of the bacteria in the skin, the procedure, in preparation for a mastoid operation for instance, consisting in the scrubbing of the previously shaven operative field with soap and water, then with benzine or ether, and finally the painting of the surface and of the adjacent hair with the mastic solution, the result being not only a firm fixation of the hair and security against its invasion of the operative field but so effectual a sterilization of the skin as to greatly favor primary healing in the cases in which it was employed.

Good Hearing after Total Destruction of the Mastoid Process by Means of a Projectile. Total Deafness, Traumatic Rupture of the Drum-head and Complete Facial Paralysis Following Concussion of the Mastoid Process.—Two contrasting cases of the effect of gunshot wounds are reported by Beck (*Monatschr. f. Ohrenh.*, 1915, xlix) as illustrative of a class of injuries now being received for investigation and treatment at base hospitals. The first patient, aged twenty-four years, had been struck by a bullet on the left mastoid process with nearly complete disruption of that bone and with passage of the projectile apparently inward and forward. On the left side of the nose there was a scar which suggested the point of exit, but there was no supporting evidence found under the Roentgen-rays and the superior maxillary on the corresponding side was free. Immediately after the injury the patient was not unconscious; he made his way unaided to the nearest dressing place and four days later was presented for examination in Vienna, very weak, with moderate degree of fever and with very purulent discharge from the external ear and from the wound in the mastoid process. Water syringed into the middle ear flowed free from the mastoid wound. Within the mastoid opening numberless small sequestræ could be easily felt and removed by means of the forceps, and after thorough cleansing of the auditory canal a fracture was determinable on the posterosuperior bony canal wall, from which place numerous granules so occluded the canal as to prevent a view of the drum-head; there was no spontaneous nystagmus. The right ear heard normally, the left ear heard a light whispered voice at a distance of seven meters and, on that side, there was complete facial paralysis in all three distributions. On the day after examination the patient had a rise of temperature with general malaise; the wound was carefully reëxamined and still more mechanical sequestræ removed. The extent of the local injury and the character of the general symptoms suggested the possibility of a sinus thrombosis, but the condition of the skin in the neighborhood of the wound indicated the beginning of erysipelas. Operative interference was deferred with the result that on the next day the erysipelas had become definitely pronounced. The later operation resulted in the removing of the sequestræ, thorough cleansing and subsequent healing, but the facial paralysis remained unchanged, and the hearing was unimproved. In the second case, of a soldier, aged twenty-two years, the projectile has entered the mouth through the right cheek and made its exit through the ear behind and under the tip of the mastoid process. The patient was unconscious for twenty-four hours after the injury. On examination there was found, in the right drum-head, in the posteroinferior quadrant, a triangular perfora-

tion with a moderate amount of discharge only. The left ear was normal of condition and of normal hearing; the right ear was completely deaf and there was complete facial paralysis. The vestibulary reaction was present as in the preceding case. This case remained five weeks under observation, during which time there was no change in the hearing and the Roentgen-ray examination of the mastoid process showed no fracture or splitting of the mastoid tip. In view of the complete paralysis of the patient and in view of the direction of the course of the projectile it is supposable that the bullet grazed the tip of the mastoid process and so severed the facial at its point of exit from the bone; the complete loss of hearing being the result of the incident shock. The contrast between this and the preceding case is that of a normal mastoid process with complete loss of hearing and of destruction of the mastoid process with a fairly good remnant of hearing.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Influence of the Exposure of the Roentgen-rays upon the Formation of Antibodies.—The destructive action of the Roentgen-rays upon the lymphatic tissues has been demonstrated by many. In part the effect of this can be shown in the diminution of the leukocytes in the blood. It has been noted that mice and guinea-pigs when exposed to the Roentgen-rays showed a variation in the susceptibility to particular infections. Some have found that the direct application of the Roentgen-ray to infected foci assisted the destruction of the bacteria. On the other hand, others were more susceptible to various infections. SIMONDS and JONES (*Jour. Med. Res.*, 1915, xxxiii, 183) carried out a series of experiments upon rabbits. These were exposed to Roentgen-rays for ten to fifteen minutes daily for a period of three weeks. They were then inoculated with B. typhosus. It appeared that the animals were less resistent to the immediate effects of the infection than the controls. In studying the antibodies quantitatively, the authors found that the production of agglutinins was appreciably less, while the quantities of bacteriolysins and opsonins were not altered to any marked degree.

Further Investigations into the Etiology of the Protozoan Disease of Turkeys, known as Black Head.—The present investigation was a continuation of the work carried on by the author in 1895. Relatively few studies have been made upon this important disease. THEOBALD SMITH (*Jour. Med. Res.*, 1915, xxxiii, 243) had previously pointed out that the pathology of the disease was not especially characteristic. The lesions are almost limited to the ceca and the liver. Occasionally too, the liver lesions may be absent. At times, however, pathological lesions are more disseminated in the intestine. The most striking feature is the filling up of the lumen with a tough leathery mould made up of concentric layers. This material may be firmly attached to the mucosa. The disease attacks both old and young, being most fatal in the first two months. The author demonstrated protozoan parasites which, to some extent, resemble and are confused with coccidia. These parasites appear in the mucosa and submucosa in which a chronic inflammation leads to much thickening. The parasites appear in large numbers lying between the cells of the various layers. The material within the bowel consists of inflammatory exudate. Similar protozoan diseases have been reported in wild and domestic birds. Animal experiments in the transmission of the disease have not been uniformly successful. Infected materials fed to healthy animals do not necessarily lead to infection. The rapid course of the disease and the lesions appear to be due as much to the mechanical disturbances accompanying the invasion and distribution of the organism as to the toxic action of the parasites. The invasion of the liver is through the blood, the parasites being transported either freely or in phagocytes. It is not known whether the parasite requires an intermediate host.

The Sterility of Bile under Normal Conditions.—TOIDA (*Arch. f. klin. Chir.*, 1914, ciii, 407) studied the character of the bile to determine the presence of organisms under normal conditions. He obtained samples of bile from 35 humans and 8 dogs. These were all sterile. He then undertook an investigation to determine the bactericidal properties of the bile. He found that B. coli could grow in fresh human bile, but were somewhat inhibited by bile from dogs. Likewise bile forms a good medium for the growth of B. typhi, which remained living ten weeks in this material. B. paratyphosus A reacts in a manner similar to B. typhi, while B. paratyphosus B and the dysentery bacillus are inhibited by the presence of bile. The B. cholera flourishes well in human bile, while B. pyocyaneus is rapidly destroyed. The staphylococci and streptococci are not greatly influenced by the bile in the medium, but pneumococci are rapidly killed off. Another interesting finding was that fresh bile appeared to enhance the virulence of B. coli.

Contribution to the Study of Endemic Goitre.—Much has been written about the endemic character of goitre. MESSERLI (*Centralbl. f. Bakteriol.*, 1914, lxxv, 3) gave water from different sources to white rats. Some were given water from the supply at Lausanne where endemic goitre is unknown, others were given water from Payerne, where goitre is very common. The latter is a surface water with a high bacterial content. The animals which were given the Lausanne water showed no changes in the thyroid, while those rats receiving water from

Payerne showed both macroscopic and microscopic evidence of thyroid hyperplasia. In various instances the enlarged thyroid could be recognized as true goitre. The author believes that his results indicate further evidence that endemic goitre is the result of improper drinking-water with definite bacterial pollution.

Basedow's Disease and the Thymus.—KOCHER (*Langenbeck's Arch.*, 1914, cv, 924) in a surgical material of 979 cases has never seen a case of Basedow's disease in which hyperplasia of the thyroid was absent. Nevertheless, a considerable number of Basedow's cases show a pathological change in the thymus. Thymus hyperplasia in Basedow's disease is more common in the young than in the old, the thymus varying in weight from 15 to 50 grams. The hyperplasia of the thymus in Basedow's is histologically similar to the not uncommon thymus hyperplasia observed in children. It is interesting that thymus hyperplasia is at times more frequent in particular families and localities than in others. It would appear that in some cases, the thymus hyperplasia is more or less coincident with a subsequent thyroid disease, and hence has no direct relation to the occurrence of Basedow's. The author suggests that the thymus hyperplasia may bear some relation to the hyperplasia of the adrenal. He believes that with the onset of Basedow's there is not uncommonly a cellular hypertrophy in the medulla of the adrenal as well as occasionally in the thymus. Some of the symptoms of Basedow's may be referable to such changes occurring in other organs. He is insistent, however, that a typical Basedow's without thyroid change and referable only to the thymus hyperplasia does not occur.

A Bacterial Study of an Epidemic of Septic Sore Throat.—An interesting epidemic of septic sore throat, traced to the milk supply of the community, is described by KRUMWEIDE and VALENTINE (*Jour. Med. Res.*, 1915, xxxiii, 231). The epidemic occurred during June, 1914, in Rockville Centre, S. I., a village of 4,250 inhabitants. The suspected milk came from a dairy (Oceanside) and supplied about 1200 quarts a day. Of the 232 cases of septic sore throat, 205 cases obtained their milk from the Oceanside dairy. In other words, the milk supply making up 25 per cent. of the total contained about 90 per cent. of the cases. On investigation, it was found that at the Oceanside dairy the daughter of the owner developed a sore throat April 16, 1914. On May 9, the owner became infected and subsequently the driver. Both the owner and the driver took care of the milking. The epidemic broke out about June 1, 1914, and lasted until about June 14. Bacteriological investigation was then undertaken including moist swabs from the throats of persons at the dairy, a culture from a complicating case of peritonitis of one of the cases, and samples of milk from each cow in the dairy. The milk obtained from five of the cows showed a moderate number of streptococci. One cow showed a mastitis, while another animal gave an enormous number of streptococci in the milk. On examining the cultures made from the cow showing the excess number of bacteria, a hemolyzing streptococcus was obtained similar in cultural characters to that obtained from the throat swabs and from that of the case of peritonitis. Cultures from the other cows

showed only non-hemolyzing types of streptococci. The facts of the case would, therefore, suggest that the infection was milk-borne, but of human origin. The cow became infected with a human type of streptococcus, although it showed no evidence of a mastitis. From these results the authors believe that in tracing such an epidemic, efforts should be made to find cases of sore throat in those engaged in milking, rather than cases of mastitis in the cows.

The Relation of the Adrenals to Cholesterin Metabolism.—A number of English authors (Ellis, Frazer, Gardner) have demonstrated that the cholesterin content of the body is in direct relation to the cholesterin intake of the food. It was shown by them that there was no cholesterin synthesis by the body tissues. On the other hand, it was demonstrated by others that a hypercholesterinemia is not uncommonly observed in pregnancy, diabetes and nephritis in which there is also a definite increase in the cholesterin content of the adrenals. This finding was interpreted by some to indicate a definite production of certain organs, particularly the adrenal of cholesterin compounds. Some experimental work was even offered to show that the adrenal had much to do with the amount of cholesterin in the blood stream. ROTHSCHILD (*Ziegler's Beitrage*, 1915, lx, 39) studied the subject experimentally, using rabbits. Because of the similar functional property of the corpus luteum cells with those of the adrenal, male animals only were used. Careful estimations were made in control animals to determine the normal quantities of cholesterin in the blood, adrenals and the bile. He then undertook the extirpation of one or both adrenals noting in each instance the variation in cholesterin content of the blood, the remaining adrenal and the bile. Upon removal of one adrenal the cholesterin content of the blood rises rapidly within twenty-four hours, while the content of the remaining adrenal is depressed during the first few days. subsequently again assuming the normal level. On removal of both adrenals, the cholesterin content of the blood rapidly increases. This would indicate that the blood cholesterin may increase without the participation of the adrenals and that the hypertrophy of the adrenal with increased cholesterin content is a secondary process. The rapid increase of cholesterin in the blood is accounted for in rapid tissue destruction or its liberation from fat depots. The cholesterin balance of the blood is maintained by the excretion of cholesterin in the bile. The author cannot find any support for the contention that the adrenals manufacture cholesterin for the body. It appears more probable that the adrenal is merely an intermediate organ which has to do with the disposal of a certain quantity of the cholesterin of the blood. His final conclusion, that Addison's disease is related to a destruction of the adrenal cortex and not its medulla, is not clear in the evidence presented.

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A Mineral Springs Health Resort and Hotel, known as THE AMERICAN NAUHEIM, from having first introduced into this country the Schott treatment for heart disease. The diagnostic and treatment methods, and the equipment embrace the best that advanced medical science has approved. Treatments are given under the direction of physicians.

THE BATHS are DIRECTLY CONNECTED WITH THE HOTEL. **The Bathing Springs are similar to the waters of Bad Nauheim, but about five times as strong. THE RADIUM EMANATION FROM BRINE SPRING NO. 2 AVERAGES 68 MACHE UNITS PER LITER OF WATER,** or nearly three times as much as any other American Spring known. For the treatment of diseases of the **Heart, Circulatory System and Kidneys; Disorders of the Nervous System; Affections of the Digestive System and Liver; "Rheumatism," Arthritis, Gout, Obesity, and Diabetes;** such symptoms as **Anaemia, Constipation, "Autointoxication," Insomnia and Neuritis, and Derangements of the Organs of Internal Secretion,** we offer advantages unsurpassed in this Country or Europe.

WINTER CONDITIONS FOR TAKING THE "CURE" OR FOR REST AND RECUPERATION ARE ESPECIALLY DESIRABLE. A natural brine—THE MOST HIGHLY RADIOACTIVE IN AMERICA—for the Nauheim Baths. Private park with miles of well-built and graded walks for Oertel hill-climbing exercise. Five minutes walk from Watkins Glen. Music, Dancing. Well-kept Golf Course, Tobogganing and Skating.

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Correspondence with physicians solicited.